

10/2008, 700  
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INVENTOR SEARCH

=> fil cap1; d que 137; fil wpix; d que 141; fil med1; d que 183; fil embase; d que 191; dup rem 137,141,191

FILE 'CAPLUS' ENTERED AT 10:14:07 ON 30 JUL 2008

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FILE COVERS 1907 - 30 Jul 2008 VOL 149 ISS 5

FILE LAST UPDATED: 29 Jul 2008 (20080729/ED)

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'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L1	1 SEA FILE=CAPLUS ABB=ON US2003-634477/AP
L2	1 SEA FILE=REGISTRY ABB=ON 11096-26-7
L3	1 SEA FILE=REGISTRY ABB=ON 209810-58-2
L7	1 SEA FILE=REGISTRY ABB=ON POLYETHYLENE GLYCOL/CN
L8	448 SEA FILE=CAPLUS ABB=ON LEHMANN P?/AU
L9	9 SEA FILE=CAPLUS ABB=ON ROEDDINGER R?/AU
L10	2183 SEA FILE=CAPLUS ABB=ON WALTER MATSUI R?/AU OR WALTER R?/AU OR MATSUI R?/AU
L11	12091 SEA FILE=CAPLUS ABB=ON L2
L12	441 SEA FILE=CAPLUS ABB=ON L2/D
L13	452 SEA FILE=CAPLUS ABB=ON L3
L15	108470 SEA FILE=CAPLUS ABB=ON L7
L16	35957 SEA FILE=CAPLUS ABB=ON PEG?/OBI
L20	29210 SEA FILE=CAPLUS ABB=ON GLYCOSYLAT?/OBI
L37	3 SEA FILE=CAPLUS ABB=ON ((L1 OR L8 OR L9 OR L10) AND ((L12 OR L13) OR (L11 AND (L15 OR L16 OR L20))))

FILE 'WPIX' ENTERED AT 10:14:08 ON 30 JUL 2008

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FILE LAST UPDATED: 24 JUL 2008 <20080724/UP>

MOST RECENT THOMSON SCIENTIFIC UPDATE: 200847 <200847/DW>

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ECLA reclassifications to April and US national classifications to the end of January 2008 have also been loaded. Update dates 20080401/UPEC and /UPNC have been assigned to these. <<<

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>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

>>> Please note that the COPYRIGHT notification has changed <<<

'BI ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

L38	882 SEA FILE=WPIX ABB=ON	WALTER MATSUI R?/AU OR WALTER R?/AU OR MATSUI R?/AU
L39	7 SEA FILE=WPIX ABB=ON	ROEDDINGER R?/AU
L40	190 SEA FILE=WPIX ABB=ON	LEHMANN P?/AU
L41	3 SEA FILE=WPIX ABB=ON	L38 AND L39 AND L40

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L71	1077 SEA FILE=MEDLINE ABB=ON	WALTER MATSUI R?/AU OR WALTER R?/AU OR MATSUI R?/AU
L72	0 SEA FILE=MEDLINE ABB=ON	ROEDDINGER R?/AU
L73	382 SEA FILE=MEDLINE ABB=ON	LEHMANN P?/AU
L74	13344 SEA FILE=MEDLINE ABB=ON	IRON METABOLISM DISORDERS+NT/CT
L75	16537 SEA FILE=MEDLINE ABB=ON	ERYTHROPOIETIN+NT/CT
L78	9965 SEA FILE=MEDLINE ABB=ON	IRON/CT(L)BL/CT
L83	0 SEA FILE=MEDLINE ABB=ON	(L71 OR L72 OR L73) AND (L75 OR L74 OR L78)

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L85	0 SEA FILE=EMBASE ABB=ON	ROEDDINGER R?/AU
L86	417 SEA FILE=EMBASE ABB=ON	LEHMANN P?/AU
L88	15072 SEA FILE=EMBASE ABB=ON	ERYTHROPOIETIN/CT OR ERYTHROPOIETIN DERIVATIVE/CT
L89	7342 SEA FILE=EMBASE ABB=ON	IRON METABOLISM DISORDER+NT/CT
L90	3643 SEA FILE=EMBASE ABB=ON	IRON BLOOD LEVEL/CT
L91	1 SEA FILE=EMBASE ABB=ON	(L84 OR L85 OR L86) AND (L88 OR L89 OR L90)

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 PROCESSING COMPLETED FOR L37  
 PROCESSING COMPLETED FOR L41  
 PROCESSING COMPLETED FOR L91  
 L93           4 DUP REM L37 L41 L91 (3 DUPLICATES REMOVED)  
               ANSWERS '1-3' FROM FILE CAPLUS  
               ANSWER '4' FROM FILE EMBASE

=> d ibib ab hitind 1-3; d iall 4

L93 ANSWER 1 OF 4 CAPLUS	COPYRIGHT 2008 ACS on STN	DUPLICATE 1
ACCESSION NUMBER:	2005:570820	CAPLUS <u>Full-text</u>
DOCUMENT NUMBER:	143:72269	
TITLE:	Use of erythropoietin or erythropoietin conjugates in the treatment of disturbances of iron distribution in chronic inflammatory intestinal diseases	
INVENTOR(S):	Klima, Horst; Lehmann, Paul; Roeddiger, Ralf; Walter-Matsui, Ruth	

PATENT ASSIGNEE(S) : F. Hoffmann-La Roche A.-G., Switz.  
 SOURCE: PCT Int. Appl., 32 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058347	A1	20050630	WO 2004-EP14105	20041210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2549486	A1	20050630	CA 2004-2549486	20041210
EP 1696947	A1	20060906	EP 2004-803748	20041210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1901934	A	20070124	CN 2004-80039809	20041210
JP 2007514673	T	20070607	JP 2006-544291	20041210
US 20050181986	A1	20050818	US 2004-13560	20041216
PRIORITY APPLN. INFO.:			EP 2003-104832	A 20031219
			WO 2004-EP14105	W 20041210

AB The present invention relates to the use of erythropoietin for the treatment of disturbances of iron distribution in chronic inflammatory intestinal diseases.

IC ICM A61K038-22

ICS A61P001-00

CC 2-10 (Mammalian Hormones)

IT 11096-26-7, Erythropoietin 11096-26-7D, Erythropoietin, conjugated, pegylated, glycosylated 25322-68-3D, Poly(ethylene glycol), erythropoietin conjugate 113427-24-0, Epoetin alfa 122312-54-3, Recormon 209810-58-2, Darbepoetin alfa

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of erythropoietin or erythropoietin conjugates in the treatment of disturbances of iron distribution in chronic inflammatory intestinal diseases)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L93 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2004:467755 CAPLUS Full-text

DOCUMENT NUMBER: 141:34188

TITLE: Methods for the use of erythropoietin and its derivatives for the treatment of heart diseases

INVENTOR(S): Lehmann, Paul; Roeddiger, Ralf;  
Walter-Matsui, Ruth

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004047858	A1	20040610	WO 2003-EP12822	20031117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20040209802	A1	20041021	US 2003-706701	20031112
CA 2505524	A1	20040610	CA 2003-2505524	20031117
AU 2003288081	A1	20040618	AU 2003-288081	20031117
AU 2003288081	B2	20070201		
EP 1565206	A1	20050824	EP 2003-779949	20031117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003016438	A	20051011	BR 2003-16438	20031117
CN 1713919	A	20051228	CN 2003-80103877	20031117
JP 2006512326	T	20060413	JP 2004-554368	20031117
RU 2324494	C2	20080520	RU 2005-119649	20031117
MX 2005PA05281	A	20050725	MX 2005-PA5281	20050517
IN 2005CN00954	A	20070810	IN 2005-CN954	20050517
KR 839302	B1	20080617	KR 2005-709185	20050520
PRIORITY APPLN. INFO.: EP 2002-26342 A 20021122 WO 2003-EP12822 W 20031117				

AB The present invention relates to the use of erythropoietin for the treatment of disturbances of iron distribution in heart diseases.

IC ICM A61K038-22

ICS A61P007-06; A61P009-04

CC 2-10 (Mammalian Hormones)

IT 11096-26-7D, Erythropoietin, conjugates and derivs. 113427-24-0,  
Epoetin alfa 122312-54-3, Epoetin beta 209810-58-2,

Darbepeoetin alfa

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(methods for use of erythropoietin (EPO) and its derivs. for treatment  
of heart diseases)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L93 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2004:203692 CAPLUS Full-text

DOCUMENT NUMBER: 140:229921

TITLE: Use of erythropoietin and analogs to treat  
disturbances of iron distribution in diabetes

INVENTOR(S): Lehmann, Paul; Roeddiger, Ralf;  
Walter-Matsui, Ruth

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004019972	A1	20040311	WO 2003-EP9194	20030820
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20040110679	A1	20040610	US 2003-634477	20030804 <--
CA 2496581	A1	20040311	CA 2003-2496581	20030820
AU 2003251713	A1	20040319	AU 2003-251713	20030820
AU 2003251713	B2	20061221		
EP 1536823	A1	20050608	EP 2003-790911	20030820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013792	A	20050712	BR 2003-13792	20030820
CN 1678341	A	20051005	CN 2003-820545	20030820
JP 2006503821	T	20060202	JP 2004-532098	20030820
RU 2305554	C2	20070910	RU 2005-108976	20030820
MX 2005PA02067	A	20050608	MX 2005-PA2067	20050222
PRIORITY APPLN. INFO.:			EP 2002-19100	A 20020829
			WO 2003-EP9194	W 20030820

AB The present invention relates to the use of erythropoietin for the treatment of disturbances of iron distribution in diabetes.

IC ICM A61K038-18

ICS A61P007-06; A61P039-00

CC 2-10 (Mammalian Hormones)

IT Protein motifs

(PEGylation sites in the Epo sequence; use of erythropoietin (Epo) and analogs to treat disturbances of iron distribution in diabetes)

IT Protein motifs

(glycosylation site, in the Epo sequence; use of erythropoietin (Epo) and analogs to treat disturbances of iron distribution in diabetes)

IT 11096-26-7, Erythropoietin 11096-26-7D, Erythropoietin, glycosylated and PEGylated variants and conjugates

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of erythropoietin (Epo) and analogs to treat disturbances of iron distribution in diabetes)

IT 113427-24-0, Epoetin alfa 122312-54-3, Epoetin beta 209810-58-2, Darbepoetin alfa

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of erythropoietin (Epo) and analogs to treat disturbances of iron distribution in diabetes)

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ACCESSION NUMBER: 1998399741 EMBASE Full-text  
 TITLE: [Porphyria cutanea tarda].  
 Porphyria cutanea tarda.

AUTHOR: Fritsch, Clemens, Dr. (correspondence); Von Schmiedeberg,  
 Sherko; Lehmann, Percy

CORPORATE SOURCE: Hautklinik der Heinrich-Heine-Univ., Moorenstrasse 5,  
 D-40225 Dusseldorf, Germany.

SOURCE: Hautarzt, (Nov 1998) Vol. 49, No. 11, pp. 870-882.  
 Refs: 91  
 ISSN: 0017-8470 CODEN: HAUTAW

COUNTRY: Germany

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT:

- 013 Dermatology and Venereology
- 022 Human Genetics
- 029 Clinical and Experimental Biochemistry
- 037 Drug Literature Index
- 005 General Pathology and Pathological Anatomy

LANGUAGE: German

ENTRY DATE: Entered STN: 17 Dec 1998  
 Last Updated on STN: 17 Dec 1998

CONTROLLED TERM:

Medical Descriptors:

- differential diagnosis
- disease association
- echography
- genetic polymorphism
  - hemochromatosis
- hepatitis b
- hepatitis c
- human
- human immunodeficiency virus infection
- liver biopsy
- \*porphyria cutanea tarda: DT, drug therapy
- \*porphyria cutanea tarda: ET, etiology
- review

CONTROLLED TERM:

Drug Descriptors:

- 5 aminolevulinate synthase: EC, endogenous compound
- alcohol
- aminotransferase: EC, endogenous compound
- chloroquine: DO, drug dose
- chloroquine: DT, drug therapy
- coproporphyrinogen: EC, endogenous compound
- deferoxamine: DT, drug therapy
- ferritin: EC, endogenous compound
- fluorouracil
- furosemide
- hexachlorobenzene
- HLA antigen class 1: EC, endogenous compound
- hydroxychloroquine: DO, drug dose
- hydroxychloroquine: DT, drug therapy
- isotretinoin
- nalidixic acid
- naproxen
- oral contraceptive agent: AD, drug administration
- porphyrin: EC, endogenous compound
- tetracycline
- transferrin: EC, endogenous compound

CAS REGISTRY NO.: uroporphyrinogen: EC, endogenous compound  
uroporphyrinogen decarboxylase: EC, endogenous compound  
(5 aminolevulinate synthase) 9037-14-3; (alcohol) 64-17-5;  
(aminotransferase) 9031-66-7; (chloroquine) 132-73-0,  
3545-67-3, 50-63-5, 54-05-7; (coproporphyrinogen)  
37293-37-1; (deferoxamine) 70-51-9; (ferritin) 9007-73-2;  
(fluorouracil) 51-21-8; (furosemide) 54-31-9;  
(hexachlorobenzene) 118-74-1, 55600-34-5;  
(hydroxychloroquine) 118-42-3, 525-31-5; (isotretinoin)  
4759-48-2; (nalidixic acid) 389-08-2; (naproxen)  
22204-53-1, 26159-34-2; (porphyrin) 24869-67-8;  
(tetracycline) 23843-90-5, 60-54-8, 64-75-5; (transferrin)  
82030-93-1; (uroporphyrinogen decarboxylase) 9024-70-8;  
(uroporphyrinogen) 35465-57-7  
CHEMICAL NAME: quensyl; resochin

TEXT SEARCH

=> fil medl

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d que 162; d que 164; d que 170; s 162,164,170 not 141
L74      13344 SEA FILE=MEDLINE ABB=ON IRON METABOLISM DISORDERS+NT/CT
L75      16537 SEA FILE=MEDLINE ABB=ON ERYTHROPOIETIN+NT/CT
L76      49008 SEA FILE=MEDLINE ABB=ON DIABETES MELLITUS, TYPE 2+NT/CT
L78      9965 SEA FILE=MEDLINE ABB=ON IRON/CT(L)BL/CT
L80      10150 SEA FILE=MEDLINE ABB=ON L75(L) (AD OR TU OR PD OR PK)/CT
SUBHEADINGS: BL=BLOOD; AD=ADMINISTRATION AND DOSAGE; TU=THERAPEUTIC USE;
PD=PHARMACOLOGY; PK=PHARMACOKINETICS
L81      1 SEA FILE=MEDLINE ABB=ON L80 AND L76 AND (L78 OR L74)
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          MELLITUS/CT
L88      15072 SEA FILE=EMBASE ABB=ON ERYTHROPOIETIN/CT OR ERYTHROPOIETIN
          DERIVATIVE/CT
L89      7342 SEA FILE=EMBASE ABB=ON IRON METABOLISM DISORDER+NT/CT
L90      3643 SEA FILE=EMBASE ABB=ON IRON BLOOD LEVEL/CT
L92      1 SEA FILE=EMBASE ABB=ON L87 AND L88 AND (L89 OR L90)
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FILE COVERS 1907 - 30 Jul 2008 VOL 149 ISS 5  
 FILE LAST UPDATED: 29 Jul 2008 (20080729/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

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<http://www.cas.org/legal/infopolicy.html>  
 'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L2	1 SEA FILE=REGISTRY ABB=ON	11096-26-7
L3	1 SEA FILE=REGISTRY ABB=ON	209810-58-2
L6	1 SEA FILE=REGISTRY ABB=ON	7439-89-6
L7	1 SEA FILE=REGISTRY ABB=ON	POLYETHYLENE GLYCOL/CN
L11	12091 SEA FILE=CAPLUS ABB=ON	L2
L13	452 SEA FILE=CAPLUS ABB=ON	L3
L14	472091 SEA FILE=CAPLUS ABB=ON	L6
L15	108470 SEA FILE=CAPLUS ABB=ON	L7
L16	35957 SEA FILE=CAPLUS ABB=ON	PEG?/OBI
L18	128446 SEA FILE=CAPLUS ABB=ON	DIABET?/OBI
L20	29210 SEA FILE=CAPLUS ABB=ON	GLYCOSYLAT?/OBI
L22	991257 SEA FILE=CAPLUS ABB=ON	IRON/OBI
L23	29660 SEA FILE=CAPLUS ABB=ON	ANEMI?/OBI
L24	6854 SEA FILE=CAPLUS ABB=ON	RETICULOCYT?/OBI
L27	12741 SEA FILE=CAPLUS ABB=ON	ERYTHROPOIETIN/OBI
L28	2577 SEA FILE=CAPLUS ABB=ON	EPO/OBI
L33	4 SEA FILE=CAPLUS ABB=ON	(L27 OR L28 OR L11) (L) (L15 OR L16 OR L20) AND L18 AND (L22 OR L23 OR L24 OR L14)
L36	4 SEA FILE=CAPLUS ABB=ON	L33 OR (L33 AND L13)

L94            3 L36 NOT L37        L37=INVENTOR SEARCH ANSWER SET

FILE 'WPIX' ENTERED AT 10:15:03 ON 30 JUL 2008  
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FILE LAST UPDATED:                    24 JUL 2008 <20080724/UP>  
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 ECLA reclassifications to April and US national classifications to the end of January 2008 have also been loaded. Update dates 20080401/UPEC and /UPNC have been assigned to these. <<<

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<http://scientific.thomsonreuters.com/support/patents/coverage/latestupdates/>

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[http://www.stn-international.com/archive/presentations/DWPAnaVist2\\_0710.pdf](http://www.stn-international.com/archive/presentations/DWPAnaVist2_0710.pdf)

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

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'BI ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

L42	2477 SEA FILE=WPIX ABB=ON	ERYTHROPOIETIN/BI, ABEX
L43	1121 SEA FILE=WPIX ABB=ON	EPO/BI, ABEX
L45	49879 SEA FILE=WPIX ABB=ON	DIABET?/BI, ABEX
L46	30843 SEA FILE=WPIX ABB=ON	PEG?/BI, ABEX
L47	51402 SEA FILE=WPIX ABB=ON	POLYETHYLENEGLYCOL/BI, ABEX OR POLY/BI, ABE X(W) (ETHYLENE GLYCOL/BI, ABEX OR ETHYLENE GLYCOL/BI, ABEX) OR POLYETHYLENE GLYCOL/BI, ABEX
L48	4420 SEA FILE=WPIX ABB=ON	GLYCOSYLAT?/BI, ABEX
L53	264038 SEA FILE=WPIX ABB=ON	IRON/BI, ABEX
L54	6529 SEA FILE=WPIX ABB=ON	ANEMI?/BI, ABEX
L55	494 SEA FILE=WPIX ABB=ON	RETICULOCYT?/BI, ABEX
L56	26 SEA FILE=WPIX ABB=ON	HEMOSIDERO?/BI, ABEX
L57	303 SEA FILE=WPIX ABB=ON	HEMOCHROMATO?/BI, ABEX
L58	29 SEA FILE=WPIX ABB=ON	HAEMOSIDERO?/BI, ABEX
L59	81 SEA FILE=WPIX ABB=ON	HAEMOCHROMATO?/BI, ABEX
L62	4 SEA FILE=WPIX ABB=ON	(L42 OR L43) (8A) (L46 OR L47 OR L48) AND L45 AND (L53 OR L54 OR L55 OR L56 OR L57 OR L58 OR L59)

L42	2477 SEA FILE=WPIX ABB=ON	ERYTHROPOIETIN/BI, ABEX
L43	1121 SEA FILE=WPIX ABB=ON	EPO/BI, ABEX
L44	12 SEA FILE=WPIX ABB=ON	DARBEPOIETIN/BI, ABEX
L53	264038 SEA FILE=WPIX ABB=ON	IRON/BI, ABEX
L63	545 SEA FILE=WPIX ABB=ON	L53 (3A) DISTRIBUT?/BI, ABEX
L64	5 SEA FILE=WPIX ABB=ON	(L42 OR L43 OR L44) AND L63

L42	2477 SEA FILE=WPIX ABB=ON	ERYTHROPOIETIN/BI, ABEX
L43	1121 SEA FILE=WPIX ABB=ON	EPO/BI, ABEX
L44	12 SEA FILE=WPIX ABB=ON	DARBEPOIETIN/BI, ABEX
L53	264038 SEA FILE=WPIX ABB=ON	IRON/BI, ABEX

L65            913 SEA FILE=WPIX ABB=ON L53 (3A) (STOR?/BI,ABEX OR METABOLI?/BI,ABE  
X)  
 L68            30878 SEA FILE=WPIX ABB=ON OVERLOAD?/BI,ABEX  
 L70            2 SEA FILE=WPIX ABB=ON (L42 OR L43 OR L44) AND L65 AND L68 NOT  
ANTIBOD?/BI,ABEX

L95            7 (L62 OR L64 OR L70) NOT L41            L41=INVENTOR SEARCH ANSWER SET

=> => dup rem 181,194,195,192  
FILE 'MEDLINE' ENTERED AT 10:15:25 ON 30 JUL 2008

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PROCESSING COMPLETED FOR L81  
PROCESSING COMPLETED FOR L94  
PROCESSING COMPLETED FOR L95  
PROCESSING COMPLETED FOR L92  
 L96            12 DUP REM L81 L94 L95 L92 (0 DUPLICATES REMOVED)  
ANSWER '1' FROM FILE MEDLINE  
ANSWERS '2-4' FROM FILE CAPLUS  
ANSWERS '5-11' FROM FILE WPIX  
ANSWER '12' FROM FILE EMBASE

=> d iall 1; d ibib ab hitind 2-4; d iall abex tech 5-11; d iall 12

L96 ANSWER 1 OF 12        MEDLINE on STN  
 ACCESSION NUMBER:        2003276465        MEDLINE Full-text  
 DOCUMENT NUMBER:        PubMed ID: 12803508  
 TITLE:                  Low dose intravenous ascorbic acid for erythropoietin-hyporesponsive anemia in diabetic hemodialysis patients with iron overload.  
 AUTHOR:                Lin Chun-Liang; Hsu Po-Yaur; Yang Huan-Yu; Huang Chiu-Ching  
 CORPORATE SOURCE:      Department of Nephrology, Chang Gung Memorial Hospital, Chia-yi, Taiwan.. linchunliang@adm.cgmh.org.tw  
 SOURCE:                Renal failure, (2003 May) Vol. 25, No. 3, pp. 445-53.  
 Journal code: 8701128. ISSN: 0886-022X.  
 PUB. COUNTRY:         United States  
 DOCUMENT TYPE:        (COMPARATIVE STUDY)  
 (Journal; Article; (JOURNAL ARTICLE))  
 LANGUAGE:              English  
 FILE SEGMENT:         Priority Journals  
 ENTRY MONTH:          200312  
 ENTRY DATE:           Entered STN: 14 Jun 2003  
 Last Updated on STN: 18 Dec 2003  
 Entered Medline: 11 Dec 2003

ABSTRACT:

BACKGROUND: Recent report demonstrates that inadequate iron mobilization and defective iron utilization may cause recombinant erythropoietin (rEPO) hyporesponsiveness in hemodialysis (HD) patients with iron overload. The effect of intravenous ascorbic acid (IVAA) in HD patients selected on the basis

of iron overload and EPO resistance also has been proven. However, it is uncertain whether IVAA still works in diabetic ESRD patients with hyperferritinemia. Therefore, the aim of this study focusing on diabetic ESRD patients was to analyze the potential effect of low dose IVAA on improvement of anemia and erythropoiesis-related parameters when compared with control period. PATIENTS AND METHOD: This study consisted of 22 chronic hemodialysis patients with type II diabetes in a single dialysis unit. In studies of this type, all eligible patients are followed up, but the primary comparison is still between different sequentially treatment including control period and post-IVAA period in same patients. IVAA patients received ascorbic acid, 100 mg each administered intravenously three times per week for eight weeks of treatment and four months of post-treatment follow-up. RESULTS: The demographic characteristics of 22 diabetic uremic patients show that mean age is 63.6 +/- 10.2 years old. The ratio of sex (M/F) = 10/12. Mean duration of HD is 46.7 +/- 33.2 months. As for the urea kinetic study between these two periods including KT/V, nPCR, and URR, there is no significantly different. As for anemia-related parameters, Hb and Hct increased significantly in post-IVAA period after 3 months compared with control period, while MCV did not increase significantly. Serum ferritin significantly decreased at study completion. The same situation is for iron. As for TS, it significantly increased at one month and further markedly increased at subsequent three months. CONCLUSION: This study has demonstrated that short-term low dose IVAA therapy can facilitate iron release from reticuloendothelial system but also increase iron utilization in diabetic hemodialysis patients with iron overload. Therefore, IVAA is a potential adjuvant therapy to treat erythropoietin-hyporesponsive anemia in iron-overloaded patients.

CONTROLLED TERM: Check Tags: Female; Male  
 Aged  
 Anemia: BL, blood  
 \*Anemia: DT, drug therapy  
 \*Ascorbic Acid: AD, administration & dosage  
 Biological Markers: BL, blood  
     Diabetes Mellitus, Type 2: BL, blood  
     \*Diabetes Mellitus, Type 2: DT, drug therapy  
 Diabetic Nephropathies: BL, blood  
 Diabetic Nephropathies: DT, drug therapy  
 Dose-Response Relationship, Drug  
 Erythrocyte Indices: DE, drug effects  
     Erythropoietin, Recombinant: AD, administration & dosage  
     \*Erythropoietin, Recombinant: TU, therapeutic use  
 Ferritins: BL, blood  
 Ferritins: DE, drug effects  
 Follow-Up Studies  
 \*Free Radical Scavengers: AD, administration & dosage  
 Hematocrit  
 Hemoglobins: DE, drug effects  
 Hemoglobins: ME, metabolism  
 Humans  
 Infusions, Intravenous  
     Iron: BL, blood  
     Iron Overload: BL, blood  
     \*Iron Overload: DT, drug therapy  
 Kidney Failure, Chronic: BL, blood  
 Kidney Failure, Chronic: DT, drug therapy  
 Middle Aged  
 Parathyroid Hormone: BL, blood  
 Phosphates: BL, blood  
 Prospective Studies  
 \*Renal Dialysis

Serum Albumin: DE, drug effects  
 Serum Albumin: ME, metabolism  
 Taiwan  
 Time Factors  
 Treatment Outcome  
 CAS REGISTRY NO.: 50-81-7 (Ascorbic Acid); 7439-89-6 (Iron); 9007-73-2  
 (Ferritins)  
 CHEMICAL NAME: 0 (Biological Markers); 0 (Erythropoietin, Recombinant); 0  
 (Free Radical Scavengers); 0 (Hemoglobins); 0 (Parathyroid  
 Hormone); 0 (Phosphates); 0 (Serum Albumin)

L96 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2008:673410 CAPLUS Full-text  
 DOCUMENT NUMBER: 149:45768  
 TITLE: Preparation of modified erythropoietin and other  
 therapeutic polypeptides with improved stability  
 INVENTOR(S): Guyon, Thierry; Borrelly, Gilles; Gallet, Xavier;  
 Drittanti, Lila; Vega, Manuel  
 PATENT ASSIGNEE(S): Nautilus Biotech, S.A., Fr.  
 SOURCE: PCT Int. Appl., 272pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008065372	A2	20080605	WO 2007-GB4520	20071127
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2006-861615P P 20061128  
 AB Modified erythropoietin (EPO) polypeptides and other modified therapeutic  
 polypeptides are provided. The EPO polypeptides and other modified  
 therapeutic polypeptides exhibit improved stability (increased resistance to  
 protease) compared with the unmodified polypeptides. Nucleic acid mols.  
 encoding these polypeptides also are provided. Also provided are  
 pharmaceutical compns. containing the modified polypeptides and methods of  
 treatment using the polypeptides. Other exemplary therapeutic polypeptides  
 include, but are not limited to interleukin-1 $\beta$ , interleukin-2, interleukin-3  
 , interleukin-4, interleukin-5, interleukin-6, interleukin-9, interferon- $\beta$ ,  
 interferon- $\gamma$ , granulocyte-colony stimulating factor, granulocyte macrophage-  
 colony stimulating factor, macrophage-colony stimulating factor,  
 thrombopoietin, leukemia inhibitory factor, stem cell factor, oncostatin M and  
 vascular endothelial growth factor.  
 CC 2-10 (Mammalian Hormones)

Section cross-reference(s) : 3, 15

IT Nerve, disease

(diabetic neuropathy; preparation of modified erythropoietin and other therapeutic polypeptides with improved resistance to proteases)

IT Retinal disease

(diabetic retinopathy; preparation of modified erythropoietin and other therapeutic polypeptides with improved resistance to proteases)

IT Adenoviral vectors

Alcoholism

Alzheimer's disease

Amnesia

Amyotrophic lateral sclerosis

Anemia

Anti-AIDS agents

Anti-Alzheimer's agents

Anti-inflammatory agents

Anti-ischemic agents

Anticonvulsants

Antiglaucoma agents

Antihypotensives

Antiparkinsonian agents

Antipsychotics

Antitumor agents

Anxiety

Anxiolytics

Buccal drug delivery systems

Cardiac arrest

Cardiopulmonary bypass

Cardiovascular agents

Central nervous system agents

Cognition enhancers

Combination chemotherapy

Controlled-release drug delivery systems

Drug delivery systems

Erythropoiesis

Genetic vectors

Glaucoma

Heart failure

Human

Hypotension

Inflammation

Ischemia

Lentiviral vectors

Molecular cloning

Mucosal drug delivery systems

Multiple sclerosis

Myocardial infarction

Nasal drug delivery systems

Neoplasm

Nervous system agents

Oral drug delivery systems

Parenteral drug delivery systems

Parkinson's disease

Pharmaceutical capsules

Pharmaceutical liquids

Pharmaceutical lozenges

Pharmaceutical tablets

Protein degradation

Protein engineering

Protein sequences

Retinal ischemia

Schizophrenia

Seizures

Stability

Stroke

Topical drug delivery systems

Transdermal drug delivery systems

Viral vectors

(preparation of modified erythropoietin and other therapeutic polypeptides with improved resistance to proteases)

IT 7439-89-6, Iron, biological studies 12629-01-5, Human growth hormone.

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(codrug; preparation of modified erythropoietin and other therapeutic polypeptides with improved resistance to proteases)

IT 9014-42-0D, Thrombopoietin, variants 11096-26-7D, Erythropoietin, variants 25322-68-3D, Polyethylene glycol, conjugates with modified therapeutic polypeptides 81627-83-0D, Macrophage-colony stimulating factor, variants 83869-56-1, Granulocyte macrophage-colony stimulating factor 83869-56-1D, Granulocyte macrophage-colony stimulating factor, variants 106956-32-5D, Oncostatin M, variants 127464-60-2D, Vascular endothelial growth factor, variants 143011-72-7D, Granulocyte-colony stimulating factor, variants

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of modified erythropoietin and other therapeutic polypeptides with improved resistance to proteases)

L96 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:448109 CAPLUS Full-text

DOCUMENT NUMBER: 148:441024

TITLE: Human erythropoietin receptor agonists, compositions, methods and uses for preventing or treating glucose intolerance-related conditions

INVENTOR(S): James, Ian E.; Picha, Kristen

PATENT ASSIGNEE(S): Centocor, USA

SOURCE: PCT Int. Appl., 89pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008042800	A2	20080410	WO 2007-US79964	20070928
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.:

US 2006-827541P

P 20060929

AB Human erythropoietin (EPO) receptor agonists are provided for preventing or treating glucose intolerance and/or renal disease associated anemia, including therapeutic compns., methods and devices. The plasma half-life of the 20-amino acid peptide EMP-1 (EPO mimetic peptide-1) was extended by construction of an EPO mimetic hinge core Mimetibody (designated CNTO 530) comprising: an N-terminal Val residue, a single copy of the bioactive EMP-1 peptide, a tandem repeat of either Gly-Ser or Gly-Gly-Gly-Ser flexible linker, a hinge core region and the CH<sub>2</sub> and CH<sub>3</sub> domains of the IgG1 or IgG4 isotype subclass. A single dose of EPO, Darbepoetin, or CNTO 530 improves glucose tolerance in mice. The extended half-life of CNTO 530 or related Mimetibodies provides several advantages as therapeutics to treat anemia and glucose intolerance in renal disease patients and for treating hyperglycemia in diabetic renal failure patients. The lack of homol. between CNTO 530 and EPO reduces the possibility of PRCA in the patient population, and the glucose tolerizing effect could minimize the requirement of this patient group for addnl. diabetes drugs.

IC ICM A61K

CC 1-10 (Pharmacology)

Section cross-reference(s): 2

ST erythropoietin receptor agonist glucose intolerance; EMP1 EPO mimetic peptide fusion IgG glucose tolerance; sequence EMP1 EPO mimetic peptide fusion IgG; anemia treatment EMP1 EPO mimetic peptide fusion IgG; hyperglycemia treatment EMP1 EPO mimetic peptide fusion IgG

IT Anemia  
 (renal, treatment of; human erythropoietin receptor agonists, compns., methods and uses for preventing or treating glucose intolerance-related conditions)

IT Diabetes mellitus  
 Hyperglycemia  
 (treatment of; human erythropoietin receptor agonists, compns., methods and uses for preventing or treating glucose intolerance-related conditions)

IT 209810-58-2, Darbepoetin-alfa  
 RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (amino acid sequence; human erythropoietin receptor agonists, compns., methods and uses for preventing or treating glucose intolerance-related conditions)

IT 11096-26-7D, Erythropoietin, variants and mimetics 25322-68-3D, Polyethylene glycol, conjugates 910576-32-8, Hematide 1019198-16-3, FG 2216 (erythropoietic agent) 1019198-38-9, FG 4592  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (human erythropoietin receptor agonists, compns., methods and uses for preventing or treating glucose intolerance-related conditions)

L96 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:12669 CAPLUS Full-text  
 DOCUMENT NUMBER: 144:465740  
 TITLE: Inappropriately low erythropoietin response for the degree of anemia in patients with noninsulin-dependent diabetes mellitus  
 AUTHOR(S): Symeonidis, Argiris; Kouraklis-Symeonidis, Alexandra; Psiroyiannis, Agathoklis; Leotsinidis, Michalis; Kyriazopoulou, Venetsana; Vassilakos, Pavlos; Vagenakis, Apostolos; Zoumbos, Nicholas  
 CORPORATE SOURCE: Hematology Division, Department of Internal Medicine, University of Patras Medical School, Patras, 261.10, Greece  
 SOURCE: Annals of Hematology (2006), 85(2), 79-85  
 CODEN: ANHEE8; ISSN: 0939-5555

PUBLISHER: Springer  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB We investigated erythropoietin (Epo) response in a cohort of diabetic patients with various types of anemia to approach the pathogenesis of some cases of "unexplained" anemia encountered among diabetics. Serum Epo levels were determined totally in 747 evaluable subjects with normal renal and hepatic function, of whom 694 had anemia. Among anemic patients, 237 were diabetics, while among the 53 nonanemic persons, there were also 21 diabetics. Diabetic and nondiabetic subjects were uniformly balanced in relation to their demog. features and were categorized according to the etiol. of their anemia. Hb (Hb) did not differ between diabetic and nondiabetic subjects in all the etiol. groups and in the whole population. Diabetic patients had significantly lower serum Epo levels as compared to nondiabetics ( $36.5 \pm 61$  vs  $69.4 \pm 191$  IU/mL,  $p < 0.0001$ ), and this was true for all etiol. groups of anemia with the exception of patients with myeloproliferative disorders and those with megaloblastic anemia. The natural logarithmic (ln)-Epo+Hb component was used as an index of response to anemia and was found to be significantly decreased in almost all subgroups of diabetic patients. Serum Epo levels were also neg. correlated with the percentage of glycosylated Hb, HbA1C ( $r = -0.446$ ), and the correlation was stronger with the ln of serum Epo ( $r = -0.638$ ,  $p < 0.001$ ). Inappropriately low serum Epo level is a uniform feature in patients with type II diabetes mellitus and may represent a constitutive blunted response to anemia or an altered metabolic rate of Epo, probably as a result of abnormal glycosylation of the cytokine.

CC 14-8 (Mammalian Pathological Biochemistry)

ST erythropoietin glycosylated Hb noninsulin dependent diabetes mellitus anemia

IT Anemia (disease)

(aplastic; serum erythropoietin level was significantly low and was neg. correlated with percentage of Hb and HbA1c in patient with noninsulin-dependent diabetes mellitus and aplastic anemia)

IT Anemia (disease)

(hemolytic; serum erythropoietin level was significantly low and was neg. correlated with percentage of Hb and HbA1c in patient with noninsulin-dependent diabetes mellitus and hemolytic anemia)

IT Anemia (disease)

(iron-deficiency; serum erythropoietin level was significantly low and was neg. correlated with percentage of Hb and HbA1c in patient with noninsulin-dependent diabetes mellitus and iron-deficiency anemia)

IT Anemia (disease)

(megaloblastic anemia; serum erythropoietin level was significantly low and was neg. correlated with percentage of Hb and HbA1c in patient with NIDDM in all anemic groups except for myeloproliferative disorder and megaloblastic anemia)

IT Diabetes mellitus

(non-insulin-dependent; serum erythropoietin level was significantly low and was neg. correlated with percentage of Hb and HbA1c in patient with NIDDM in all anemic groups except for myeloproliferative disorder and megaloblastic anemia)

IT Human

Myeloproliferative disorders

(serum erythropoietin level was significantly low and was neg. correlated with percentage of Hb and HbA1c in patient with NIDDM in all anemic groups except for myeloproliferative disorder and megaloblastic anemia)

IT Hemoglobins

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
 (serum erythropoietin level was significantly low and was neg. correlated with percentage of Hb and HbA1c in patient with NIDDM in all anemic groups except for myeloproliferative disorder and megaloblastic anemia)

IT Myelodysplastic syndromes  
 (serum erythropoietin level was significantly low and was neg. correlated with percentage of Hb and HbA1c in patient with noninsulin-dependent diabetes mellitus and myelodysplastic syndrome)

IT Thalassemia  
 ( $\beta$ -; serum erythropoietin level was significantly low and was neg. correlated with percentage of Hb and HbA1c in patient with noninsulin-dependent diabetes mellitus and  $\beta$ -thalassemia caused anemia)

IT 62572-11-6, Hemoglobin A1c  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
 (serum Epo level was significantly low and was neg. correlated with percentage of Hb and glycosylated Hb in patient with NIDDM in all anemic groups except for myeloproliferative disorder and megaloblastic anemia)

IT 11096-26-7, Erythropoietin  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
 (serum erythropoietin level was significantly low and was neg. correlated with percentage of Hb and HbA1c in patient with NIDDM in all anemic groups except for myeloproliferative disorder and megaloblastic anemia)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L96 ANSWER 5 OF 12 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN  
 ACCESSION NUMBER: 2006-099173 [10] WPIX  
 DOC. NO. CPI: C2006-035289 [10]  
 TITLE: New constrained bicyclic cyano compounds are dipeptidyl peptidase inhibitors useful for treating e.g. restenosis, HIV infection, multiple sclerosis, retinopathy, nephropathy, Syndrome X, diabetes and anemia  
 DERWENT CLASS: B02; B05  
 INVENTOR: BETANCORT J M; CAMPBELL D A; WINN D; WINN D T; BETANCORT J; CAMPBELL D  
 PATENT ASSIGNEE: (BETA-I) BETANCORT J M; (CAMP-I) CAMPBELL D A; (WINN-I) WINN D T; (PHEN-N) PHENOMIX CORP  
 COUNTRY COUNT: 110

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20060009518	A1	20060112	(200610)*	EN	35[0]	
WO 2006017292	A1	20060216	(200613)	EN		
EP 1778220	A1	20070502	(200731)	EN		
JP 2008505975	W	20080228	(200817)	JA	76	

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20060009518	A1 Provisional	US 2004-587391P	20040712
US 20060009518	A1	US 2005-179797	20050712
EP 1778220	A1	EP 2005-773420	20050712
WO 2006017292	A1	WO 2005-US24695	20050712
EP 1778220	A1	WO 2005-US24695	20050712
JP 2008505975	W	WO 2005-US24695	20050712
JP 2008505975	W	JP 2007-521571	20050712

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1778220	A1	WO 2006017292
JP 2008505975	W	WO 2006017292

PRIORITY APPLN. INFO: US 2005-179797 20050712  
US 2004-587391P 20040712

## INT. PATENT CLASSIF.:

MAIN: A61K031-40

IPC ORIGINAL: A61K0031-275 [I,C]; A61K0031-277 [I,A]; A61K0031-40 [I,A];  
; A61K0031-40 [I,C]; A61K0031-429 [I,A]; A61K0031-429 [I,C]; A61K0045-00 [I,A]; A61K0045-00 [I,C]; A61P0001-00 [I,C]; A61P0001-02 [I,A]; A61P0001-04 [I,A]; A61P0001-14 [I,A]; A61P0001-18 [I,A]; A61P0013-00 [I,C]; A61P0013-08 [I,A]; A61P0013-12 [I,A]; A61P0015-00 [I,A]; A61P0015-00 [I,C]; A61P0015-08 [I,A]; A61P0019-00 [I,C]; A61P0019-02 [I,A]; A61P0019-10 [I,A]; A61P0025-00 [I,A]; A61P0025-00 [I,C]; A61P0025-28 [I,A]; A61P0029-00 [I,A]; A61P0029-00 [I,C]; A61P0003-00 [I,A]; A61P0003-00 [I,C]; A61P0003-04 [I,A]; A61P0003-06 [I,A]; A61P0003-08 [I,A]; A61P0003-10 [I,A]; A61P0031-00 [I,C]; A61P0031-18 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0035-04 [I,A]; A61P0037-00 [I,A]; A61P0037-00 [I,C]; A61P0037-02 [I,A]; A61P0043-00 [I,A]; A61P0043-00 [I,C]; A61P0005-00 [I,C]; A61P0005-06 [I,A]; A61P0005-28 [I,A]; A61P0007-00 [I,C]; A61P0007-06 [I,A]; A61P0009-00 [I,A]; A61P0009-00 [I,C]; A61P0009-10 [I,A]; A61P0009-12 [I,A]; C07D0487-00 [I,A]; C07D0487-00 [I,C]; C07D0513-00 [I,C]; C07D0513-04 [I,A]

ECLA:

C07D0513-04+277C+209C

USCLASS NCLM:

514/522.000

NCLS: 558/410.000

## BASIC ABSTRACT:

US 20060009518 A1 UPAB: 20060224

NOVELTY - Constrained bicyclic cyano compounds (I) are new.

DETAILED DESCRIPTION - Constrained bicyclic cyano compounds of formula (I) and their stereoisomers, solvates, hydrates, tautomers, prodrugs, salts or mixtures are new. X = CRR', S, O or CR;

R1 and R4 = H, alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, cycloalkenyl, (cycloalkenyl)alkyl, aryl, aralkyl, heterocyclyl or heterocyclylalkyl (where alkyl, alkenyl and alkynyl and the alkyl moieties of the (cycloalkyl)alkyl, (cycloalkenyl)alkyl, aralkyl, and heterocyclylalkyl groups are optionally mono to tri-substituted by O, NH, S, SO, SO<sub>2</sub> or a 3, 4, 5, or 6 member divalent carbocyclyl or heterocyclyl group); R, R', R<sub>2</sub>, R<sub>3</sub>, R<sub>5</sub> and R<sub>6</sub> = H, halo, ORa, NRaRb, CN, NO<sub>2</sub>, C(O)Ra, C(O)ORb, C(O)NRaRb, NHC(O)Ra, NHC(O)ORA or optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, cycloalkenyl, (cycloalkenyl)alkyl, aryl, aralkyl,

heterocyclyl, or heterocyclylalkyl (where the alkyl, alkenyl and alkynyl groups and the alkyl moieties of the (cycloalkyl)alkyl, (cycloalkenyl)alkyl, aralkyl, and heterocyclylalkyl are optionally mono to tri-substituted by O, NH, S, SO, SO<sub>2</sub> or a 3, 4, 5, or 6 member divalent carbocyclyl or heterocyclyl); R<sub>2</sub>+R<sub>5</sub> and R<sub>3</sub>+R<sub>6</sub> = oxo; and Ra and Rb = H, optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, cycloalkenyl, (cycloalkenyl)alkyl, aryl, aralkyl, heterocyclyl or heterocyclylalkyl group. Provided that X is CR, when it forms a double bond with one of the carbons to which it is attached. INDEPENDENT CLAIMS are included for the following:

(1) intermediate bicyclic compound of formula (II) that is an 8-membered bicyclic heterocycle comprising a pyrrolidinonyl ring, that is substituted with a cyano group and a basic group having a pKa of from about 6 to about 10, and inhibits dipeptidyl peptidase-IV with a Ki of 10 μM or less;

(2) preparation of (I); and (3) a pharmaceutical combination (C1) comprising (I) and at least one compound selected from other dipeptidyl peptidase-IV inhibitors; insulin sensitizers selected from PPAR agonists, biguanides, and protein phosphatase-1B inhibitors; insulin or insulin mimetics; sulfonylureas or other insulin secretagogues; alpha-glucosidase inhibitors; glucagons receptor agonists; GLP-1, GLP-1 mimetics, and GLP-1 receptor agonists; GIP, GIP mimetics, and GIP receptor agonists; PACAP, PACAP mimetics, and PACAP receptor 3 agonists; GLP-2, GLP-2 mimetics, and GLP-2 receptor agonists; cholesterol lowering agents selected from HMG-CoA reductase inhibitors, sequestrants, nicotinyl alcohol, nicotinic acid or their salts, PPAR-alpha agonists, PPAR-alpha/gamma dual agonists, inhibitors of cholesterol absorption, acyl CoA:cholesterol acyltransferase inhibitors, and anti-oxidants; PPAR-delta agonists; anti-obesity compounds; ileal bile acid transporter inhibitor; anti-inflammatory agents; G-CSF, G-CSF mimetics, and G-CSF receptor agonists; and EPO, EPO mimetics, and EPO receptor agonists.

ACTIVITY - Antidiabetic; Anorectic; Antilipemic; Antiarteriosclerotic; Vasotropic; Antiinflammatory; Gastrointestinal-Gen.; Endocrine-Gen.; Anti-HIV; Neuroprotective; Ophthalmological; Analgesic; Antianginal; Immunosuppressive; Immunostimulant; Antianemic; Cytostatic; Hypotensive; Osteopathic; Antiinfertility; Gynecological; Anabolic; Eating-Disorders-Gen.; Antiulcer; Antiarthritic; Antirheumatic.

MECHANISM OF ACTION - Dipeptidyl peptidase DPP (e.g. DPP-IV, DPP-VII, DPP-VIII and DPP-IX) inhibitor. The efficacy of 6-amino-5-oxo-hexahydro-pyrrolo(2,1-b)thiazole-3-carbonitrile hydrochloride (Iaa) as inhibitor of DPP-IV was evaluated using fluorometric assay with the substrate Gly-Pro-AMC. (Iaa) Was dissolved in DMSO or in 50 mM glycine buffer (pH 3). The assay was performed by diluting the DPP-IV stock (10 μl) into 25 mM Tris buffer (77.5 μl) followed by addition of (Iaa) (2.5 μl) at 26 degrees C. After 10 minutes, substrate was added (10 μl) and allowed to react for 20 minutes at 26 degrees C before free (7-amino-4-methyl coumarin) (AMC) was measured and the IC<sub>50</sub> value was determined. (Iaa) Showed an IC<sub>50</sub> value of less than or equal to 100 μM.

USE - For treating conditions mediated by dipeptidyl peptidase-IV inhibition such as insulin resistance, hyperglycemia, low glucose tolerance, insulin resistance, obesity, lipid disorders; atherosclerosis, vascular restenosis, irritable bowel syndrome, inflammatory conditions, growth hormone deficiency, HIV infection, pancreatitis, abdominal obesity, neurodegenerative disease, multiple sclerosis, retinopathy, nephropathy, neuropathy, Syndrome X, ovarian hyperandrogenism, allograft rejection in transplantation, diabetes, neutropenia, anemia, neuronal disorders, tumor growth and metastasis, benign prostatic hypertrophy, gingivitis, hypertension, osteoporosis, dysmetabolic syndrome, diabetic complications, impaired glucose homeostasis, infertility, polycystic ovary syndrome, growth disorders, frailty, autoimmune diseases, intestinal diseases, anorexia nervosa; lipid disorders such as dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL, or high

LDL; inflammatory condition such as inflammatory bowel disease, Crohn's disease, ulcerative colitis, rheumatoid arthritis (claimed).

**ADVANTAGE** - The compound is greater than or equal to 90 weight% of a single diastereomer or enantiomer. The compounds inhibits dipeptidyl peptidase-IV greater than 5-fold relative to other dipeptidyl peptidases such as dipeptidyl peptidase-VII, dipeptidyl peptidase-VIII, dipeptidyl peptidase-IX, fibroblast activation protein, dipeptidyl peptidase-VIII and fibroblast activation protein, dipeptidyl peptidase-VII, dipeptidyl peptidase-VIII, and fibroblast activation protein. The treatment provides islet neogenesis, beta-cell survival or enhanced insulin biosynthesis. MANUAL CODE: CPI: B01-D02; B04-J03A; B06-E03; B06-F03; B06-H; B07-H;

B14-A02B1; B14-C01; B14-C03; B14-C06; B14-C09; B14-D01;  
B14-D02; B14-D07C; B14-E08; B14-E10; B14-E11; B14-E12;  
B14-F01; B14-F01D; B14-F02B; B14-F02D; B14-F03; B14-F06;  
B14-F07; B14-F09; B14-G02; B14-G03; B14-H01; B14-N01;  
B14-N03; B14-N04; B14-N06B; B14-N07A; B14-N10; B14-N11;  
B14-N13; B14-N14; B14-N16; B14-P02; B14-S01; B14-S04;  
B14-S13

**ABEX DEFINITIONS** - Preferred Definitions: - X = CH<sub>2</sub>, S or O; - R1 = H, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, cyclopentyl, cyclopentyl-(CH<sub>2</sub>)-, cyclohexyl, cyclohexyl-(CH<sub>2</sub>)-, phenyl, benzyl, phenylethyl, imidazolyl-(CH<sub>2</sub>)- or indolyl-(CH<sub>2</sub>)- (all optionally mono- or di-substituted by F, Cl, Br, I, hydroxy, oxo, cyano, amino, methylamino, dimethylamino, azido, nitro, 1-4C alkoxy, trifluoromethyl, trifluoromethoxy, carboxyl, carboxamido, SH, S(O)O-2CH<sub>3</sub> or guanidino); - R4 = H; and - R2, R3, R5 and R6 = H, F, Cl, OH, or optionally substituted 1-6C alkyl, phenyl or benzyl.

**ADMINISTRATION** - Dosage is 0.05 - 1000 (preferably 0.5 - 500) mg. The route of administration is oral, nasal, pulmonary, buccal, subdermal, intradermal, transdermal or parenteral (e.g. rectal, depot, subcutaneous, intravenous, intraurethral, intramuscular, intranasal or ophthalmic).

**SPECIFIC COMPOUNDS** - 13 Compounds are specifically claimed as (I), e.g. 6-amino-5-oxo-hexahydro-pyrrolo(2,1-b)thiazole-3-carbonitrile hydrochloride (Iaa).

**EXAMPLE** - Burgess reagent (0.8 g, 3.3 mmol) was added in solution of (3-carbamoyl-5-oxo-hexahydro-pyrrolo(2,2-b)thiazol-6-yl)-carbamic acid tert-butyl ester (0.5 g) in dry tetrahydrofuran (20 ml) at room temperature. The mixture was washed, dried and purified to produce (3-Cyano-5-oxo-hexahydro-pyrrolo(2,1-b)thiazol-6-yl)-carbamic acid tert-butyl ester (a). (a) Was dissolved in 2N HCl/dioxane (15 ml) with stirring. After 2 hours, white solid formed. The clear liquid was removed and another dry ethyl ether (20 ml) was added, stirred and then discarded to obtained 6-amino-5-oxo-hexahydro-pyrrolo(2,1-b)thiazole-3-carbonitrile hydrochloride(Iaa) (0.12 g, yield 26%).

#### TECH

**ORGANIC CHEMISTRY** - Preparation (claimed): Preparation of (I) involves exposing an amide compound of formula (III) to a dehydrating agent such as trifluoroacetic anhydride or methyl N-(triethylammoniosulfonyl)carbamate followed by removing the amino protecting group(s).

R4a=amino protecting group; and

R4a+R4=cyclic amino protecting group.

**PHARMACEUTICALS** - Preferred Combination: (C1) Further comprises a carrier. In (C1), the at least one compound is an HMG-CoA reductase inhibitor, or an antidiabetic agent. (C1) Further comprises an anti-obesity agent, a lipid-modulating agent, or both an anti-obesity agent and a lipid-modulating agent, and wherein the antidiabetic agent other than dipeptidyl peptidase-IV inhibitor. In the treatment of neutropenia, the method further involves administering a neutrophilic agent. In the treatment of anemia, the method further involves administering an erythropoietin agonist. In (C1), (I) is present in 0.01 - 100:1 weight

ratio to the antidiabetic agent or to the lipid-modulating agent. Preferred Components: The HMC-CoA reductase inhibitor is a statin selected from lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, itavastatin, ZD-4522 and rivastatin. The neutrophilic agent is G-CSF, G-CSF mimetic and/or G-CSF receptor agonist (preferably pegfilgrastim, filgrastim, lenograstim and/or nartograstim. The erythropoietin agonist is EPO, EPO mimetic and/or EPO receptor agonist (preferably epoetin alfa, darbepoetin alfa). The antidiabetic agent is at least one compound selected from biguanide, sulfonyl urea, glucosidase inhibitor, PPAR-gamma agonist, PPAR-alpha/gamma dual agonist, SGLT2 inhibitor, aP2 inhibitor, glycogen phosphorylase inhibitor, AGE inhibitor, insulin sensitizer, glucagon-like peptide-1 (GLP-1) or mimetic, insulin and meglitinide (preferably metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, APR-HO39242, GW-409544, KRP297, AC2993, Exendin-4, LY307161, NN2211 or LY315902). The anti-obesity agent is beta 3 adrenergic agonist, lipase inhibitor, serotonin (and dopamine) reuptake inhibitor, thyroid receptor beta compound, anorectic agent and/or fatty acid oxidation upregulator (preferably orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, famoxin and/or mazindol). The lipid-modulating agent is MTP inhibitor, HMG CoA reductase inhibitor, squalene synthetase inhibitor, fibric acid derivative, upregulator of LDL receptor activity, lipoxygenase inhibitor, ACAT inhibitor, cholestryl ester transfer protein inhibitor and/or ATP citrate lyase inhibitor (preferably pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, nisvastatin, visastatin, fenofibrate, gemfibrozil, clofibrate, implitapide, CP-529414, avasimibe, TS-962, MD-700 and/or LY295427).

L96 ANSWER 6 OF 12 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN  
 ACCESSION NUMBER: 2003-371843 [35] WPIX  
 DOC. NO. CPI: C2003-098688 [35]  
 DOC. NO. NON-CPI: N2003-296569 [35]  
 TITLE: Determining iron status and detecting iron metabolism disorders, comprises determining parameters that allow determination of total body iron stores, erythropoietic maturation process and unspecific disorders of iron metabolism  
 DERWENT CLASS: B04; S03  
 INVENTOR: LEHMANN P; RODDIGER R; ROEDDINGER R; THOMAS L  
 PATENT ASSIGNEE: (HOFF-C) HOFFMANN LA ROCHE & CO AG F; (LEHM-I) LEHMANN P;  
 (HOFF-C) ROCHE DIAGNOSTICS GMBH; (RODD-I) RODDIGER R;  
 (THOM-I) THOMAS L  
 COUNTRY COUNT: 27

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003025583	A2	20030327	(200335)*	EN	26 [4]	
US 20030073635	A1	20030417	(200335)	EN		
US 20030232393	A1	20031218	(200401)	EN		
EP 1425589	A2	20040609	(200438)	EN		
JP 2005503559	W	20050203	(200516)	JA	47	
EP 1425589	B1	20071205	(200782)	EN		
DE 60223931	E	20080117	(200807)	DE		
DE 60223931	T2	20080403	(200825)	DE		
EP 1909106	A2	20080409	(200827)	EN		

ES 2297011 T3 20080501 (200833) ES

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003025583	A2	WO 2002-EP10250	20020912
US 20030073635	A1 Provisional	US 2001-322526P	20010914
US 20030232393	A1 Provisional	US 2001-322526P	20010914
DE 60223931	E	DE 2002-60223931	20020912
DE 60223931	T2	DE 2002-60223931	20020912
EP 1425589	A2	EP 2002-777081	20020912
EP 1425589	B1	EP 2002-777081	20020912
DE 60223931	E	EP 2002-777081	20020912
DE 60223931	T2	EP 2002-777081	20020912
EP 1909106	A2 Div Ex	EP 2002-777081	20020912
US 20030073635	A1	US 2002-242061	20020912
US 20030232393	A1 CIP of	US 2002-242061	20020912
EP 1425589	A2	WO 2002-EP10250	20020912
JP 2005503559	W	WO 2002-EP10250	20020912
EP 1425589	B1	WO 2002-EP10250	20020912
DE 60223931	E	WO 2002-EP10250	20020912
DE 60223931	T2	WO 2002-EP10250	20020912
JP 2005503559	W	JP 2003-529161	20020912
US 20030232393	A1	US 2003-449633	20030530
EP 1909106	A2	EP 2007-23170	20020912
ES 2297011	T3	EP 2002-777081	20020912

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
DE 60223931	E	EP 1425589
DE 60223931	T2	EP 1425589
EP 1909106	A2	EP 1425589
EP 1425589	A2	WO 2003025583
JP 2005503559	W	WO 2003025583
EP 1425589	B1	WO 2003025583
DE 60223931	E	WO 2003025583
DE 60223931	T2	WO 2003025583
ES 2297011	T3	EP 1425589

PRIORITY APPLN. INFO: US 2001-322526P 20010914  
                           US 2002-242061 20020912  
                           US 2003-449633 20030530

## INT. PATENT CLASSIF.:

MAIN:	G01N033-72
SECONDARY:	C12Q001-28; C12Q001-30; G01N033-52; G01N033-68; G01N033-90
IPC ORIGINAL:	G01N0033-84 [I,A]; G01N0033-84 [I,A]; G01N0033-84 [I,C]; G01N0033-84 [I,C]; G01N0033-90 [I,A]; G01N0033-90 [I,C]
IPC RECLASSIF.:	C12Q0001-28 [I,A]; C12Q0001-28 [I,C]; C12Q0001-30 [I,A]; C12Q0001-30 [I,C]; G01N0033-52 [I,A]; G01N0033-52 [I,C]; G01N0033-68 [I,A]; G01N0033-68 [I,C]; G01N0033-72 [I,A]; G01N0033-72 [I,C]; G01N0033-80 [I,A]; G01N0033-80 [I,C]; G01N0033-90 [I,A]; G01N0033-90 [I,C]
ECLA:	G01N0033-80; G01N0033-90
USCLASS NCLM:	435/007.100
NCLS:	436/066.000; 436/518.000
BASIC ABSTRACT:	

WO 2003025583 A2 UPAB: 20050903

NOVELTY - Determining the iron status and in particular detecting disorders of iron metabolism, comprises determining a parameter (P1) which allows a determination of the total body iron stores, a parameter (P2) which allows a determination of the erythropoietic maturation process and/or its activity, and a parameter (P3) which allows a determination of unspecific disorders of iron metabolism.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a test strip comprising an unit for performing the above method.

USE - The method is useful for carrying out differential diagnosis of disorders of iron metabolism, and for classifying disorders of iron status and disorders of iron metabolism. The method is also useful for observing and/or monitoring progress and/or response to treatment (all claimed). The method is useful for diagnosing chronic diseases and chronic inflammatory diseases, particularly rheumatoid arthritis, renal insufficiency, malignancies, diabetes, heart failure, cardiovascular disease, neurodegenerative diseases, impaired pregnancies and thrombosis, and for diagnosing disorders associated with iron overloading e.g. sickle cell anemia.

ADVANTAGE - The method provides rapid and reliable information on the iron status of patients. The combination of independent parameters enables a routine differentiation between normal iron status, iron deficiency, iron distribution disorders and/or iron overloading. The method also allows a differentiation between normal iron status and iron overloading and allows a differentiation between the status of iron deficiency and iron distribution disorders. The method also allows a sex-specific discrimination or differentiation of the individual iron status in which the normal values or cut-off values can then be established for each sex (male or female). MANUAL CODE: CPI: B04-B04D2; B04-C01; B04-H02A; B04-H02G; B04-H02M;

B04-H05; B04-H06G; B04-H06K; B04-H08; B04-H19; B04-J03A;  
B04-L03; B04-L03B; B04-N02; B04-N06; B05-A03B; B06-D18;  
B11-C08; B12-K04A  
EPI: S03-E04E; S03-E14H

ABEX EXAMPLE - 373 patients were examined using a combination of hematological parameters and biochemical parameters and classified into four groups.

Group N was the control group and contained non-anemic patients without acute phase reaction (APR). Group A consisted of anemic patients without APR. Group AA contained anemic patients with APR in combination with cancer-related anemia (CRA), anemia of chronic disease (ACD) or an acute infectious or inflammatory disease. The patient group NA-contained non-anemic patients with APR. Ferritin was determined and the reference range was determined as 20-150 mug/l for women and 20-350 mug/l for men. Serum-circulating transferrin receptor (TfR) was determined in each sample using commercial assays. The analytical principle of the assay was based on microagglutination of latex particles which were coated with a monoclonal anti-TfR antibody. Percentage transferrin saturation (TfS) was calculated using the formula TfS (%) = Fe(mug/l)x7.09/Tf (g/l). In order to determine disorders of iron metabolism, hemoglobin content of reticulocytes (CHr) and proportion of hypochromic red cells (HRC%) were determined as indicators of an iron deficient erythropoiesis as a plot against the TfR-F index. - The following results were obtained for the individual patient groups. N group (non-anemic group without APR): The control group consisted of 71 patients and had a CHr of at least 28 pg, a group (anemic group without APR): 79 anemic patients without APR were examined and were diagnosed as iron-deficient according to the TfR-F index. All patients had a HRC greater than 5% the pattern CHr greater than 288 pg, HRC greater than 5%, elevated TfR and normal or elevated ferritin indicated that these patients with CRA and APR had a reduced iron supply as indicated by the increase in TfR which, however, was not sufficient to cause a functional iron deficiency. NA group (non-anemic group with APR): The group consisted of 80 patients which had a CHr of less than 28 pg and

a HRC of greater than 5%. AA group (anemic group with APR) consisted of 143 patients which had the lowest ferritin and highest Tf concentrations. Tf is a negative acute phase reactant the mean concentration was reduced in patients. - The patient groups were subdivided as follows according to the hematological and biochemical results: Group N: non-anemic, no APR; hemoglobin (Hb) (men) at least 140 g/l, Hb (women) at least 123 g/l, C-reactive protein (CRP) upto 5 mg, white blood cell (WBC) upto 10000/mul, ESR (erythrocyte sedimentation rate) upto 30 mm/hour, RDW (red cell distribution width) upto 15%; Group A: anemic, no APR; Hb (men) less than 140 g/l, Hb (women) less than 123 g/l, CRP upto 5 mg, white blood cell (WBC) upto 10000/mul, ESR upto 30 mm/hour; Group NA: non-anemic, with APR; Hb (men) at least 140 g/l, Hb (women) at least 123 g/l, CRP greater than 5 mg or WBC greater than 10000/mul or ESR greater than 30 mm/hour, or RDW greater than 15%; AA: anemic with APR; Hb (men) less than 140 g/l, Hb (women) less than 123 g/l, CRP greater than 5 mg or WBC greater than 10000/mul or ESR greater than 30 mm/hour.

## TECH

BIOLOGY - Preferred Method: P1 Comprises erythrocyte ferritin, zinc protoporphyrin, hemoglobin, myoglobin, transferrin, transferrin saturation, ferritin, hemosiderin, catalase, peroxidase and/or cytochrome. P2 Comprises erythrocyte indices, reticulocyte indices, FS-e (forward scatter erythrocytes) and/or soluble transferrin receptor (sTfR). P3 Comprises acute phase proteins, in particular C-reactive protein (CRP), serum amyloid A (SAA), alpha<sub>1</sub>-antichymotrypsin, acidic alpha<sub>1</sub>-glycoprotein, alpha<sub>1</sub>-antitrypsin, haptoglobin, fibrinogen, complement component C3, complement component C4 or ceruloplasmin, and/or regulators of acute phase protein synthesis in particular interleukin 6 (IL-6), leukemia inhibiting factor (LIF), oncostatin M, IL-11, ciliary neurotropic factor (CNTF), IL-1alpha, IL-1beta, tumor necrosis factor-alpha (TNFalpha), TNFbeta, insulin, fibroblast growth factor (FGF), hepatocyte growth factor, transforming growth factor beta (TGFbeta) or interferon (IFN) and/or disorders of reticulocyte synthesis in particular reticulocyte count, hemoglobin (Hb) content of reticulocyte (CHR), immature reticulocyte fraction (IRF), new red blood cell (RBC) and reticulocyte fluorescence parameters or forward scatter reticulocytes (FS-r). Preferably, P3 is a hematological parameter, especially Chr. The method involves determination of a parameter which allows a determination of the total body iron stores, a parameter which allows determination of erythropoietic maturation process and/or its activity, and a parameter which allows a determination of unspecific disorders of iron metabolism, in particular a biochemical parameter, and a hematological parameter.

The iron status is classified into one of the following groups: (A) iron distribution disorders and/or iron utilization disorders with acute phase reaction, (B) iron overloading, (C) normal iron status, and (D) deficiency of storage iron. Based on the classification of the disorder of iron metabolism, a required treatment is recommended, e.g. an erythropoietin (EPO) therapy is indicated for a classification in group (A), blood letting is indicated for a classification in group (B), no therapy is indicated for a classification in group (C), and iron substitution is indicated when classified in group (D).

L96 ANSWER 7 OF 12 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

ACCESSION NUMBER: 2002-257594 [30] WPIX

DOC. NO. CPI: C2002-076696 [30]

TITLE: New method useful for the treatment of e.g. fatigue, pain, chronic heart failure involves the use of a recombinant erythropoietin

DERWENT CLASS: B04; D16

INVENTOR: ALTHOFF C; THOMPSON L H; THOMPSON L  
 PATENT ASSIGNEE: (ALTH-I) ALTHOFF C; (BAXT-C) BAXTER HEALTHCARE SA;  
 (THOM-I) THOMPSON L H  
 COUNTRY COUNT: 95

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002014356	A2	20020221	(200230)*	EN	88 [26]	
AU 2001091755	A	20020225	(200245)	EN		
EP 1317276	A2	20030611	(200339)	EN		
CZ 2003000406	A3	20030618	(200347)	CS		
KR 2003034134	A	20030501	(200357)	KO		
BR 2001013189	A	20030916	(200369)	PT		
HU 2003000740	A2	20030929	(200369)	HU		
JP 2004506652	W	20040304	(200417)	JA	142	
MX 2003001237	A1	20041101	(200558)	ES		
CN 1636014	A	20050706	(200574)	ZH		
US 7078376	B1	20060718	(200648)	EN		
RU 2282460	C2	20060827	(200657)	RU		
NZ 542370	A	20060929	(200667)	EN		
AU 2001291755	B2	20060518	(200681)	EN		
AU 2006203640	A1	20060914	(200712) #	EN		
NZ 524000	A	20070629	(200746)	EN		
EP 1317276	B1	20071107	(200778)	EN		
DE 60131286	E	20071220	(200802)	DE		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002014356	A2	WO 2001-EP9209	20010809
US 7078376	B1	US 2000-637962	20000811
AU 2001091755	A	AU 2001-91755	20010809
AU 2001291755	B2	AU 2001-291755	20010809
AU 2006203640	A1 Div Ex	AU 2001-291755	20010809
BR 2001013189	A	BR 2001-13189	20010809
CN 1636014	A	CN 2001-817002	20010809
EP 1317276	A2	EP 2001-971896	20010809
EP 1317276	B1	EP 2001-971896	20010809
NZ 542370	A Div Ex	NZ 2001-524000	20010809
NZ 524000	A	NZ 2001-524000	20010809
NZ 542370	A	NZ 2001-542370	20010809
EP 1317276	A2	WO 2001-EP9209	20010809
CZ 2003000406	A3	WO 2001-EP9209	20010809
BR 2001013189	A	WO 2001-EP9209	20010809
HU 2003000740	A2	WO 2001-EP9209	20010809
JP 2004506652	W	WO 2001-EP9209	20010809
MX 2003001237	A1	WO 2001-EP9209	20010809
RU 2282460	C2	WO 2001-EP9209	20010809
NZ 524000	A	WO 2001-EP9209	20010809
EP 1317276	B1	WO 2001-EP9209	20010809
JP 2004506652	W	JP 2002-519493	20010809
CZ 2003000406	A3	CZ 2003-406	20010809
HU 2003000740	A2	HU 2003-740	20010809
RU 2282460	C2	RU 2003-106435	20010809
KR 2003034134	A	KR 2003-701938	20030210
MX 2003001237	A1	MX 2003-1237	20030210
AU 2006203640	A1	AU 2006-203640	20060817

EP 1317276 B1 Related to EP 2007-75711 20070822  
DE 60131286 E DE 2001-631286 20010809  
DE 60131286 E EP 2001-971896 20010809  
DE 60131286 E WO 2001-EP9209 20010809

**FILING DETAILS:**

PATENT NO	KIND		PATENT NO
NZ 542370	A	Div ex	NZ 524000
AU 2001091755	A	Based on	WO 2002014356
EP 1317276	A2	Based on	WO 2002014356
CZ 2003000406	A3	Based on	WO 2002014356
BR 2001013189	A	Based on	WO 2002014356
HU 2003000740	A2	Based on	WO 2002014356
JP 2004506652	W	Based on	WO 2002014356
MX 2003001237	A1	Based on	WO 2002014356
RU 2282460	C2	Based on	WO 2002014356
AU 2001291755	B2	Based on	WO 2002014356
NZ 524000	A	Based on	WO 2002014356
EP 1317276	B1	Based on	WO 2002014356
DE 60131286	E	Based on	EP 1317276
DE 60131286	E	Based on	WO 2002014356

PRIORITY APPLN. INFO: US 2000-637962 20000811  
AU 2006-203640 20060817

INT. PATENT CLASSIF.:

MAIN: A61K038-00; A61K038-18; A61K038-22; C07K014-00

**SECONDARY:** A61K033-24; A61P001-18; A61P025-00; A61P035-00;

A61P037-06; A61P009-00

IPC ORIGINAL: A61K0038-00 [I,A]; A61K0038-18 [I,A]; A61K0038-18 [I,C];  
A61K0038-18 [I,A]; A61K0038-18 [I,C]; A61K0038-18 [I,A];  
A61K0038-18 [I,C]; A61P0025-00 [I,A]; A61P0025-00 [I,C];  
A61P0025-00 [I,A]; A61P0025-00 [I,C]; A61P0009-00 [I,A];  
A61P0009-00 [I,C]; A61P0009-00 [I,A]; A61P0009-00 [I,C];  
C07K0014-00 [I,A]; C07K0014-00 [I,C]; C07K0014-435 [I,C];  
C07K0014-505 [I,A]; C12N0015-00 [I,A]; C12N0015-00 [I,C];  
C12N0005-00 [I,A]; C12N0005-00 [I,C]

IPC RECLASSIF.: A61K0033-24 [I,A]; A61K0033-24 [I,C]; A61K0038-00 [I,A];  
A61K0038-00 [I,C]; A61K0038-18 [I,A]; A61K0038-18 [I,C];  
A61P0001-00 [I,C]; A61P0001-18 [I,A]; A61P0025-00 [I,A];  
A61P0025-00 [I,C]; A61P0035-00 [I,A]; A61P0035-00 [I,C];  
A61P0037-00 [I,C]; A61P0037-06 [I,A]; A61P0009-00 [I,A];  
A61P0009-00 [I,C]; C07K0014-435 [I,C]; C07K0014-47 [I,A]

ECLA: A61K0038-18B

USCLASS NCLM: 514/002.000

NCI-S: 435/069-100

**BASIC ABSTRACT:** 155,355.100, 155,356.100, 155,357.100, 355,357.100

WO 2003014

WO 2002014358 A2 UPAB: 20060202

NOVELTY - Use of a recombinant erythropoietin for the manufacture of a medicament for prevention or treatment of fatigue, pain, chronic heart failure, dysrhythmia or dementia, is new. ACTIVITY - Nootropic; Neuroprotective; Cardiant; Analgesic; Antiarthritic; Cytostatic; Hypotensive; Immunosuppressive; Antianemic; Hepatotropic; Anti-inflammatory; Virucide; Thrombolytic. A 71 year old man displayed congestive heart failure, coronary artery disease and generalized arteriosclerosis. The patient was also suffering from adenocarcinoma of the lung and colon was presented with an iron deficiency anemia and suffered from chronic fatigue among other symptoms, and having a history of diabetic mellitus and myocardial infection. Primary treatment of both the lung cancer and the colon cancer included resection. The

patient was treated with LASIX (RTM) and LISINOPRIL (RTM) to manage the blood pressure, since he was hypertensive. At intake, the patient had a hemoglobin count of 12.9, on HCT count of 39.6% and platelet count of 213K. During the course of the cancer therapy, the patient was administered Epoetin Omega at a dose of 3x2000 IU/wk, which corresponded to about 100 IU/kg/week at 33 IU/kg per administration. There was no significant increase in blood pressure, no thrombotic effects and no worsening of cardiac function. The response of the subject indicates that even for a patient having conditions such as hypertension, chronic heart failure and coronary artery disease associated with cancer that are counter-indicated for treatment with Epoetin Alpha. The use of Epoetin Omega did not exacerbate preexisting hypertension nor produce any thrombotic episodes.

MECHANISM OF ACTION - None given in the source material.

USE - For the manufacture of a medicament for prevention or treatment of fatigue, pain (e.g. vascular pain), chronic heart failure, dysrhythmia (e.g. jet lag) or dementia and for treatment of a symptom (e.g. anemia, fatigue and vascular pain, all associated with a cancer therapy such as chemotherapy (preferably cisplatin therapy or radiation therapy) having a condition (e.g. hypertension, thrombosis, heart condition, cancer, an autoimmune disease, liver dysfunction, hepatitis and treatment by chemotherapy or radiation therapy adversely effected by a side effect of treatment with erythropoietin. The fatigue and the vascular pain to be treated, are associated with a cancer, liver dysfunction, hepatitis infection, heart condition, autoimmune disease (e.g. arthritis), chronic fatigue syndrome, and a cancer therapy (e.g. chemotherapy such as cisplatin therapy and radiation therapy) and the chronic heart failure to be treated, is associated with renal failure and/or diabetic condition of a patient, cancer and/or cancer therapy (all claimed).

ADVANTAGE - The therapeutic amount of the recombinant erythropoietin doses not elicit anti-erythropoietin IgG antibodies over a treatment period of 4 - 16 weeks, provides a therapeutic benefit such as increased red blood cells, increased HCT (undefined), increased hemoglobin, increased vigor, increased mental acuity or decreased pain within a treatment period without producing or exacerbating any adverse side effects (e.g. increased blood sugar, hypertension thrombosis and increased platelet count) associated with treatment by a Epoetin Alpha or Beta.

MANUAL CODE:

CPI: B04-H0700E; B14-C01; B14-C03; B14-C09; B14-F01;  
B14-F02; B14-F02B; B14-F03; B14-F04; B14-G02D; B14-H01;  
B14-J01; B14-J01A; B14-J01A2; B14-N12; B14-S04;  
D05-H17A2; D05-H17A6

ABEX ADMINISTRATION - The medicament is administered subcutaneously. The erythropoietin is administered before, during or after the cancer therapy. The recombinant erythropoietin is administered at a dose 5 - 150 (preferably 55 - 150) IU/kg, 1 - 3 times per week; 75 - 200 IU/Kg, once per week, 10 - 200 IU/kg, 1 - 3 times per week or 25 - 50 IU/kg, 1 - 3 times and for treatment of dysrhythmia, it is administered at a dose of 25 - 50 IU/kg, 1 - 3 times (claimed).

TECH

PHARMACEUTICALS - Preferred Compounds: The recombinant erythropoietin is Epoetin Omega, an erythropoietin produced in baby hamster kidney cells, an erythropoietin expressed from an Apa I restriction fragment of human genomic erythropoietin DNA, an erythropoietin having a glycosylation pattern which is having the presence of N-linked glycosylate residues on at least three asparagine residues, an erythropoietin having an O-linked oligosaccharide content of less than 1 mole per mole of glycoprotein, an erythropoietin having at least one isoforms at isoelectric points of 4.3, 4.5 or 4.6 or a recombinant erythropoietin that retains substantially all of its in vitro biological activity after being subject to N-deglycosylation (preferably Epoetin Omega).

ACCESSION NUMBER: 2003-209426 [20] WPIX  
 CROSS REFERENCE: 1999-609314; 2003-478799  
 DOC. NO. CPI: C2003-053285 [20]  
 TITLE: Use of recombinant human erythropoietin for treatment of patient with vascular damage  
 DERWENT CLASS: B04  
 INVENTOR: ZAHARIA V C  
 PATENT ASSIGNEE: (ZAHIA-I) ZAHARIA V C  
 COUNTRY COUNT: 1

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20020169129	A1	20021114	(200320)*	EN	4 [0]	

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20020169129	A1 CIP of	US 1998-18815	19980204
US 20020169129	A1 Provisional	US 1998-91598P	19980702
US 20020169129	A1 Provisional	US 1999-125253P	19990319
US 20020169129	A1 Div Ex	US 1999-335076	19990617
US 20020169129	A1 Provisional	US 2001-287206P	20010428
US 20020169129	A1 CIP of	US 2001-872630	20010601
US 20020169129	A1	US 2002-133545	20020426

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 20020169129	A1 CIP of	US 5951996 A
US 20020169129	A1 Div ex	US 6274158 B

PRIORITY APPLN. INFO:	US 2002-133545	20020426
	US 1998-18815	19980204
	US 1998-91598P	19980702
	US 1999-125253P	19990319
	US 1999-335076	19990617
	US 2001-287206P	20010428
	US 2001-872630	20010601

## INT. PATENT CLASSIF.:

IPC RECLASSIF.: A61K0038-12 [N,A]; A61K0038-12 [N,C]; A61K0038-18 [I,A];  
 A61K0038-18 [I,C]

ECLA: A61K0038-18B

ICO: K61K0038:12

USCLASS NCLM: 514/012.000

## BASIC ABSTRACT:

US 20020169129 A1 UPAB: 20050528

NOVELTY - In the treatment of a patient with vascular damage, recombinant human erythropoietin (RhuEPO) is used. ACTIVITY - Antidiabetic; Antiarteriosclerotic; Neuroprotective; Nootropic; Hemostatic; Immunosuppressive; Antianemic; Vulnerary; Tranquilizer; Anticoagulant. MECHANISM OF ACTION - None given.

USE - In the treatment of a patient with vascular damage (e.g. vasculitis capillary leak syndrome, aneurysms, chemical or physical damage to vessel) due to vesicant drugs (e.g. Adriamycin or vincristin) with catastrophic extravasation of the vesicant drug and ongoing chemical burn in thrombotic thrombocytopenic purpura (TTP) or hemolytic uremic syndrome (HUS) e.g.

Alzheimer's disease. Also useful for limiting chronic blood loss (all claimed). The vascular damage also includes diseases e.g. diabetes, arteriosclerotic or other damage to vessels leading to overt bleeding or oozing of blood cerebral bleeding, aneurysms, damage to blood vessels caused by traumatic, chemical or physical agents or postoperatively.

**ADVANTAGE** - (RhuEPO) increases the quality of life of the patient (prior to an increase in hemoglobin (Hb) of 1 g/dl), which includes improvement in appetite, increase in patient's weight, sense of physical and mental well being prior to any change in the Hb/Hematocrit, better physical tolerance to daily life's demands, less shortness of breath, less fatigue and less palpitations, increased capacity to walk and work for longer periods of time, improvement in their cognitive function, of mood, clearing of sensorium, becoming more alert and a more rapid and appropriate response to questions. (RhuEPO) brings improvement in cognitive functions in patients regardless of their hemoglobin (Hb) level; can be administered topically to patients with superficial bleeding lesions with enhancement of the hemostatic process; prevents iron loss and channels the saved iron directly into the erythroid precursor leading to increased Hb level, increased MCH, and increased RBC hemaglobinisation; traps iron in the reticuloendothelial system in patients with anemia of chronic disease or hematologic malignancy made available to erythropoiesis; controls better bleeding processes resulting from shortening of the bleeding time in chronic renal failure patients on hemodialysis as well as in patients with normal kidney function; can be administered topically on a limited part of a bleeding lesion and results in the bleeding in that area stopping earlier than the natural cessation of bleeding in areas where no (RhuEPO) is applied; is used in iron overload conditions to unload the iron trapped in nonhemic cells (non-erythropoietic); can exogenously be administered in anemia of chronic disease patients having normal endogenous levels of erythropoietin; can be administered during anticoagulation with Heparin, warfarin or aspirin to repair damaged vascular wall and lead to efficient and lasting hemostasis despite continuation of anticoagulation at therapeutic or several times the therapeutic range for anticoagulation; can work at the platelet subendothelial level to promote primary plug formation and repair damaged vessels; decreases the protein C, protein S and Antithrombin III level; can be administered to a patient with congenital hemolytic anemias (RhuEPO) to stimulate the production of new RBC's, removes excessive iron accumulated in the body and channels the excess iron in the new RBC's. (RhuEPO) leads to the redistribution of the iron trapped in storage organs, where it cannot be used for red blood cell production, into the hemopoietic system leading to enhanced red blood cell production. The treatment induces excellent compliance with the treatment itself as a result of the fact that patients and their families are aware of the physical and psychological improvements induced by (RhuEPO). **MANUAL CODE:** CPI: B04-N0600E; B14-F02; B14-F03; B14-F04; B14-F07;

B14-F08; B14-G02; B14-J01A4; B14-N17B; B14-S04

**ABEX ADMINISTRATION** - (RhuEPO) is administered topically (claimed). No dosages are given.

**EXAMPLE** - A patient was administered Aspirin, Heparin and Coumadin for an acute myocardial infarct. The patient was difficult to control and developed PT and PTT often several times the normal value. An enlarging massive retroperitoneal bleeding developed compromising the kidney function. After administering packed red blood cells (5 units), fresh frozen plasma (9 units), and vitamin K injections, the bleeding continued. Then recombinant human erythropoietin (RhuEPO) injection (512 U/kg/week) was given to the patient and observed that the bleeding stopped and never recurred. Thus RhuEPO enhanced hemostasis, boosted hemopoiesis (i.e. increase in hemoglobin (Hb) of 3.7/20 g/dl) and raised the MCH (i.e. increase in MCH (pg)/time (days) 2.1/20) with no side effects.

TITLE: Erythropoietin (EPO) primary response gene 1 polypeptides, useful for treating anemia, cytopenia, cancer, obesity, infection, AIDS, autoimmune diseases, diabetes and multiple sclerosis

DERWENT CLASS: B04; D16

INVENTOR: DILLON S B; KING A G; LORD K A

PATENT ASSIGNEE: (SMIK-C) SMITHKLINE BEECHAM CORP

COUNTRY COUNT: 20

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001029178	A2	20010426	(200130)*	EN	40[0]	
EP 1224220	A2	20020724	(200256)	EN		
JP 2003520577	W	20030708	(200347)	JA	56	

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001029178	A2	WO 2000-US29072	20001019
EP 1224220	A2	EP 2000-975323	20001019
EP 1224220	A2	WO 2000-US29072	20001019
JP 2003520577	W	WO 2000-US29072	20001019
JP 2003520577	W	JP 2001-532164	20001019

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1224220	A2	Based on WO 2001029178 A
JP 2003520577	W	Based on WO 2001029178 A

PRIORITY APPLN. INFO: US 1999-422153 19991021

## INT. PATENT CLASSIF.:

MAIN: C12N015-09

IPC RECLASSIF.: A61K0031-7088 [I,A]; A61K0031-7088 [I,C]; A61K0038-00 [I,A]; A61K0038-00 [I,C]; A61K0039-395 [I,A]; A61K0039-395 [I,C]; A61K0045-00 [I,A]; A61K0045-00 [I,C]; A61K0048-00 [I,A]; A61K0048-00 [I,C]; A61P0011-00 [I,C]; A61P0011-06 [I,A]; A61P0025-00 [I,A]; A61P0025-00 [I,C]; A61P0029-00 [I,A]; A61P0029-00 [I,C]; A61P0003-00 [I,C]; A61P0003-04 [I,A]; A61P0003-10 [I,A]; A61P0031-00 [I,A]; A61P0031-00 [I,C]; A61P0031-00 [I,A]; A61P0031-18 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0037-00 [I,C]; A61P0037-02 [I,A]; A61P0037-08 [I,A]; A61P0043-00 [I,A]; A61P0043-00 [I,C]; A61P0005-00 [I,A]; A61P0005-00 [I,C]; A61P0007-00 [I,C]; A61P0007-06 [I,A]; C07K0014-435 [I,C]; C07K0014-47 [I,A]; C07K0016-18 [I,A]; C07K0016-18 [I,C]; C12N0001-15 [I,A]; C12N0001-15 [I,C]; C12N0001-15 [I,C]; C12N0001-19 [I,A]; C12N0001-19 [I,C]; C12N0001-21 [I,A]; C12N0001-21 [I,C]; C12N0015-09 [I,A]; C12N0015-09 [I,C]; C12N0005-10 [I,A]; C12N0005-10 [I,C]; C12P0021-02 [I,A]; C12P0021-02 [I,C]; C12Q0001-02 [I,A]; C12Q0001-02 [I,C]; C12Q0001-02 [I,C]; C12Q0001-68 [I,A]; C12Q0001-68 [I,C]; G01N0033-15 [I,A]; G01N0033-15 [I,C]; G01N0033-50 [I,A]; G01N0033-50 [I,C]; G01N0033-50 [I,C]; G01N0033-566 [I,A]; G01N0033-566 [I,C]

ECLA: C07K0014-47

ICO: K61K0038:00; M07K0207:00

**BASIC ABSTRACT:**

WO 2001029178 A2 UPAB: 20050525

**NOVELTY** - An EPO (erythropoietin) primary response gene 1 (EPRG1) polypeptide (I) comprising a sequence having at least 70%, preferably 95%, identity to a 157 amino acid sequence (S1) defined in the specification, a sequence comprising S1, or S1, is new.

**DETAILED DESCRIPTION** - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide (II) comprising: (a) a sequence encoding (I); (b) a sequence comprising a nucleotide sequence having at least 70%, preferably 95%, identity to a sequence encoding S1; (c) a sequence having at least 70%, preferably 95%, identity to a sequence (S2) comprising 2111 nucleotides fully defined in the specification;

(d) a sequence comprising a nucleotide sequence encoding S1, (e) the sequence of S2;

(f) a sequence obtained by screening an appropriate library under stringent hybridization conditions with a labeled probe having S2 or its fragment, or its complement;

(2) an antibody (Ab) immunospecific for (I); (3) diagnosing a disease or susceptibility to a disease in a subject related to expression or activity of (I) in a subject, by determining the presence or absence of a mutation in (II) in the genome of the subject and/or analyzing for the presence or amount of expression of (I) in a sample derived from the subject; (4) screening to identify compounds which stimulate or inhibit the function of (I), by:

(a) measuring the binding of a candidate compound (CC) to (I) (or to the cells or membranes bearing (I)) or a fusion protein comprising (I), using a label, directly or indirectly associated with CC; (b) measuring the competition of binding of CC to (I) (or to the cells or membranes bearing (I)) or a fusion protein comprising (I), in the presence of a labeled competitor; (c) testing whether CC results in a signal generated by activation or inhibition of (I), using detection systems appropriate to the cells or membranes bearing (I);

(d) mixing CC with a solution containing (I) to form a mixture, measuring activity of (I) in the mixture, and comparing the activity of the mixture to a control mixture which contains no CC; or (e) detecting the effect of CC on the production of mRNA encoding (I), or (I) in cells, using for instance, an ELISA assay; (5) an agonist or antagonist of (I); (6) an expression system (III) comprising a polynucleotide capable of producing (I), when present in a compatible host cell; (7) producing a recombinant host cell, by transforming or transfecting a cell with (III), such that under appropriate culture condition, produces (I);

(8) a recombinant host cell (IV) produced by the above said method;

(9) a membrane (V) of (IV), expressing (I); (10) producing (I) by culturing (IV); (11) an isolated polynucleotide comprising: (a) a sequence having at least 70%, preferably 97% identity to a sequence (S3) comprising 711 or 2342 nucleotides fully defined in the specification

(b) a sequence comprising S3 (c) the sequence of S3; or

(d) a polynucleotide complementary to the sequences of (a)-(c); (12) an EPRG1 inhibitor (VI), which is an ASO (antisense oligonucleotide) comprising a sequence gaccatggcgcacggagcca or gctgtgggtgaccatggcgc; and

(13) an ASO comprising a sequence gaccatggcgcacggagcca or gctgtgggtgaccatggcgc.

**ACTIVITY** - Cytostatic; anti-HIV; antianemic; immunosuppressive; antiasthmatic; antiallergic; antirheumatic; antiarthritic; antidiabetic; neuroprotective. No supporting biological data given.

**MECHANISM OF ACTION** - Gene therapy; vaccine. No supporting biological data given.

**USE** - (I), (II) and agonist of (I) are useful for treatment of a subject in need of enhanced activity or expression of (I). Antagonist of (I), a nucleic acid molecule that inhibits the expression of (II) or a polypeptide that competes with (I) for its ligand, is useful for the treatment of a subject having a need to inhibit activity or expression of (I). (VI) is useful for treating cytopenia along

with cytokines such as G-CSF (granulocyte colony stimulating factor), EPO, TPO, interleukin 11 (IL-11), IL-3, PEG-rHuMGDF, FLT-3, NESP, or NEUPOGEN SD. (VI) is also useful for increasing the effectiveness and engraftment of a hematopoietic stem cell transplantation by mixing (VI) with a solution containing hematopoietic progenitor and stem cells, ex vivo, followed by transplantation of the hematopoietic cells into a patient in need of, mixing (VI) with a solution containing hematopoietic cells in an ex vivo stem cell expansion culture system followed by transplantation of the hematopoietic cells into the patient, or by administering (VI) in vivo as an adjunct to hematopoietic stem cell transplantation or during the treatment of cytopenia. (VI) is also useful for increasing the efficiency of gene therapy transfer into hematopoietic stem cells, by isolating hematopoietic stem cells or modified stem cell lines, and incubating with (VI) before transfection with plasmid vectors containing any corrective gene of interest useful in treating a hereditary genetic disease (claimed). (I) and (II) are useful for treating and diagnosing cytopenias including anemia, neutropenia and thrombocytopenia, polycythemia, cancer, metabolic or genetic growth deficiencies, obesity, infection by immunostimulation, infectious disease or cancer by adjuvant enhancement of vaccine therapy, AIDS, drug-induced anemias, autoimmune diseases, such as rheumatoid arthritis, diabetes, multiple sclerosis, and inflammatory diseases such as asthma and allergies. (II) is useful for chromosomal localization studies and as valuable tools for tissue expression studies. (I) and (II) are useful as vaccines.

MANUAL CODE: CPI: B04-C01G; B04-E03F; B04-E06; B04-E08; B04-F0100E; B04-F1100E; B04-G01; B04-N02A; B11-C07; B11-C08; B12-K04A; B12-K04E; B12-K04F; B14-A01; B14-A02; B14-E12; B14-F02; B14-F03; B14-G02A; B14-H01; B14-J01; B14-K01A; B14-L01; B14-L06; B14-S01; B14-S03; B14-S11; D05-H07; D05-H08; D05-H09; D05-H11; D05-H12A; D05-H12D2; D05-H12E; D05-H14; D05-H17A6

ABEX WIDER DISCLOSURE - The following are disclosed as new: - (1) a diagnostic kit for performing a diagnostic assay comprising (I), (II), their complements or Ab; - (2) a screening kit for screening agonist, antagonist, ligand, receptor, substrate, enzyme, etc., of (I), comprises (I), (IV), (V) or Ab; - (3) EPRG1 antisense oligonucleotides; and - (4) a pharmaceutical composition comprising EPRG1 polypeptide.

ADMINISTRATION - 0.1-100 mug of (I) is administered through systemic, oral or topical route.

EXAMPLE - No relevant example given.

#### TECH

BIOTECHNOLOGY - Preparation: (I) is produced by culturing (IV) and recovering (I) from the culture medium (claimed).

L96 ANSWER 10 OF 12	WPIX COPYRIGHT 2008	THOMSON REUTERS on STN
ACCESSION NUMBER:	1999-036814 [04]	WPIX
DOC. NO. CPI:	C1999-011170 [04]	
TITLE:	Use of erythropoietin and modified haemoglobin - to treat anaemia	
DERWENT CLASS:	B04	
INVENTOR:	FEUERSTEIN J; LEHMANN P; TOWN M; TOWN M H; TOWN M -	
PATENT ASSIGNEE:	(BOEF-C) BOEHRINGER MANNHEIM GMBH; (FEUE-I) FEUERSTEIN J; (LEHM-I) LEHMANN P; (HOFF-C) ROCHE DIAGNOSTICS GMBH; (TOWN-I) TOWN M H	
COUNTRY COUNT:	79	

#### PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA	PG	MAIN IPC
<hr/>					
EP 885613	A1 19981223 (199904)*	DE	5	[0]	
WO 9858660	A1 19981230 (199907)	DE			

AU 9881098	A	19990104	(199921)	EN
EP 996462	A1	20000503	(200026)	DE
BR 9810267	A	20000912	(200051)	PT
CN 1261282	A	20000726	(200057)	ZH
MX 9911664	A1	20000601	(200133)	ES
KR 2001014075	A	20010226	(200154)	KO
JP 2002504913	W	20020212	(200215)	JA 16
AU 743475	B	20020124	(200221)	EN
US 6440932	B1	20020827	(200259)	EN
US 20020160956	A1	20021031	(200274)	EN
EP 996462	B1	20040804	(200451)	DE
DE 59811768	G	20040909	(200459)	DE
ES 2226151	T3	20050316	(200525)	ES
US 20050197281	A1	20050908	(200559)	EN
CN 1185010	C	20050119	(200620)	ZH
MX 235274	B	20060329	(200651)	ES
KR 519904	B	20051010	(200680)	KO
JP 2007246530	A	20070927	(200765)	JA 8
CA 2294448	C	20071211	(200802)	EN

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 885613	A1	EP 1997-110168	19970621
AU 9881098	A	AU 1998-81098	19980603
AU 743475	B	AU 1998-81098	19980603
BR 9810267	A	BR 1998-10267	19980603
CN 1261282	A	CN 1998-806432	19980603
CN 1185010	C	CN 1998-806432	19980603
DE 59811768	G	DE 1998-511768	19980603
EP 996462	A1	EP 1998-930785	19980603
EP 996462	B1	EP 1998-930785	19980603
DE 59811768	G	EP 1998-930785	19980603
ES 2226151	T3	EP 1998-930785	19980603
WO 9858660	A1	WO 1998-EP3299	19980603
EP 996462	A1	WO 1998-EP3299	19980603
BR 9810267	A	WO 1998-EP3299	19980603
JP 2002504913	W	WO 1998-EP3299	19980603
US 6440932	B1	WO 1998-EP3299	19980603
EP 996462	B1	WO 1998-EP3299	19980603
DE 59811768	G	WO 1998-EP3299	19980603
MX 235274	B	WO 1998-EP3299	19980603
KR 519904	B	WO 1998-EP3299	19980603
JP 2002504913	W	JP 1999-503655	19980603
JP 2007246530	A Div Ex	JP 1999-503655	19980603
MX 9911664	A1	MX 1999-11664	19991214
MX 235274	B	MX 1999-11664	19991214
KR 2001014075	A	KR 1999-712111	19991221
KR 519904	B	KR 1999-712111	19991221
US 6440932	B1	US 2000-446378	20000207
US 20020160956	A1 Cont of	US 2000-446378	20000207
US 20050197281	A1 Cont of	US 2000-446378	20000207
US 20020160956	A1	US 2002-140682	20020508
US 20050197281	A1 Cont of	US 2002-140682	20020508
US 20050197281	A1	US 2005-91876	20050328
JP 2007246530	A	JP 2007-113275	20070423
CA 2294448	C	CA 1998-2294448	19980603
CA 2294448	C	WO 1998-EP3299	19980603

## FILING DETAILS:

PATENT NO	KIND	PATENT NO	
AU 743475	B	Previous Publ	AU 9881098
DE 59811768	G	Based on	EP 996462
ES 2226151	T3	Based on	EP 996462
KR 519904	B	Previous Publ	KR 2001014075
US 20020160956	A1	Cont of	US 6440932
US 20050197281	A1	Cont of	US 6440932
AU 9881098	A	Based on	WO 9858660
EP 996462	A1	Based on	WO 9858660
BR 9810267	A	Based on	WO 9858660
JP 2002504913	W	Based on	WO 9858660
AU 743475	B	Based on	WO 9858660
US 6440932	B1	Based on	WO 9858660
EP 996462	B1	Based on	WO 9858660
DE 59811768	G	Based on	WO 9858660
MX 235274	B	Based on	WO 9858660
KR 519904	B	Based on	WO 9858660
CA 2294448	C	Based on	WO 9858660

PRIORITY APPLN. INFO: EP 1997-110168 19970621  
                           WO 1998-EP3299 19980603

## INT. PATENT CLASSIF.:

MAIN: A61K038-16; A61K038-42

SECONDARY: A01N037-18; A01N038-00; A61K038-00

IPC ORIGINAL: A61K0038-18 [I,A]; A61K0038-18 [I,C]; A61K0038-22 [I,A];  
                   A61K0038-22 [I,C]; A61K0038-41 [I,C]; A61K0038-42 [I,A];  
                   A61P0007-00 [I,C]; A61P0007-06 [I,A]

IPC RECLASSIF.: A61K0038-16 [I,A]; A61K0038-16 [I,C]; A61K0038-18 [N,A];  
                   A61K0038-18 [N,C]; A61K0038-22 [I,A]; A61K0038-22 [I,C];  
                   A61K0038-41 [I,C]; A61K0038-42 [I,A]; A61P0007-00 [I,C];  
                   A61P0007-06 [I,A]

ECLA: A61K0038-42+M

USCLASS NCLM: 514/006.000

NCLS: 514/006.000; 514/012.000

## BASIC ABSTRACT:

EP 885613 A1 UPAB: 20060114 Use of modified haemoglobin and erythropoietin (EPO) for treatment of anaemia is new.

ADVANTAGE - The modified haemoglobin serves as an intravenous iron replacer and it can be infused in large amounts (corresponding to 100-200 mg of Fe<sup>2+</sup>), avoiding circulatory reactions associated with Fe(III) salts.

MANUAL CODE: CPI: B04-B04D2; B04-H07; B14-F03

L96 ANSWER 11 OF 12 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

ACCESSION NUMBER: 1988-149159 [22] WPIX

DOC. NO. CPI: C1988-066442 [21]

TITLE: Erythropoietin, especially recombinant prod. - used in medicament for reducing stored iron and serum iron in mammal with iron overload disorder

DERWENT CLASS: B04

INVENTOR: ADAMSON J W; DOWNING M R; EGRIE J C; ESCHBACH J W  
                   (AMGE-N) AMGEN; (KIRI-C) KIRIN AMGEN INC

PATENT ASSIGNEE: 23

## PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA	PG	MAIN IPC
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EP 269394	A	19880601	(198822)*	EN	5[0]
WO 8803808	A	19880602	(198823)	EN	
JP 63159322	A	19880702	(198832)	JA	
AU 8781794	A	19880616	(198836)	EN	
DK 8804074	A	19880721	(198848)	DA	
PT 86187	A	19881215	(198907)	PT	
US 5013718	A	19910507	(199121)	EN	
EP 269394	B	19911016	(199142)	EN	
DE 3773852	G	19911121	(199148)	DE	
IL 84275	A	19930404	(199318)	EN	
ES 2039252	T3	19930916	(199342)	ES	
CA 1322165	C	19930914	(199343)	EN	
DK 167650	B	19931206	(199403)	DA	
JP 06092316	B2	19941116	(199444)	JA 4	
KR 9509100	B1	19950814	(199843)	KO	

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 269394 A		EP 1987-310300	19871120
US 5013718 A		US 1986-933495	19861121
WO 8803808 A		WO 1987-US2673	19871019
DK 167650 B		WO 1987-US2673	19871019
KR 9509100 B1		WO 1987-US2673	19871019
IL 84275 A		IL 1987-84275	19871025
CA 1322165 C		CA 1987-552139	19871118
JP 63159322 A		JP 1987-293071	19871119
JP 06092316 B2		JP 1987-293071	19871119
ES 2039252 T3		EP 1987-310300	19871120
DK 167650 B		DK 1988-4074	19880721
KR 9509100 B1		KR 1988-700864	19880721

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
DK 167650 B	Previous Publ	DK 8804074 A
ES 2039252 T3	Based on	EP 269394 A
JP 06092316 B2	Based on	JP 63159322 A

PRIORITY APPLN. INFO: US 1986-933495 19861121

INT. PATENT CLASSIF.:

MAIN: A61K037-24

IPC RECLASSIF.: A61K0038-00 [I,A]; A61K0038-00 [I,C]; A61K0038-18 [I,A];  
A61K0038-18 [I,C]; A61K0038-22 [I,A]; A61K0038-22 [I,C];  
A61P0003-00 [I,A]; A61P0003-00 [I,C]; A61P0007-00 [I,A];  
A61P0007-00 [I,C]

ECLA: A61K0038-18B

USCLASS NCLM: 514/008.000

NCLS: 514/002.000; 514/021.000; 604/006.020; 604/500.000;  
604/507.000

## BASIC ABSTRACT:

EP 269394 A UPAB: 20050428 Use of erythropoietin (I) for the manufacture of a medicament for therapeutic application for reducing stored Fe and serum Fe in a mammal having a Fe overload disorder. Pref the (I) may be obtained by recombinant DNA methods. It is administered at 15 units/kg or higher doses, esp at 50-300 units/kg. USE/ADVANTAGE - A mammal having a Fe overload disorder is given a medicament comprising (I) and phlebotomised to remove excess of red blood cells.

The procedure effectively reduces stored Fe and serum Fe to normal levels.  
 MANUAL CODE: CPI: B04-B04H; B12-J05

L96 ANSWER 12 OF 12 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004370545 EMBASE Full-text  
 TITLE: Erythropoietin in the treatment of patients with type 2 diabetes mellitus and anemia.  
 AUTHOR: Pavkovic, Pajica (correspondence); Mrzljak, Vladimir; Profozic, Velimir; Metelko, Zeljko  
 CORPORATE SOURCE: Vuk Vrhovac Institute, Univ. Clin. Diabet., Endocr./M. D., Dugi dol 4a, HR-10000 Zagreb, Croatia.  
 SOURCE: Diabetologia Croatica, (2004) Vol. 33, No. 1, pp. 13-16.  
 Refs: 15  
 ISSN: 0351-0042 CODEN: DBCRB2  
 COUNTRY: Croatia  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 025 Hematology  
                   028 Urology and Nephrology  
                   003 Endocrinology  
                   037 Drug Literature Index  
                   006 Internal Medicine  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 16 Sep 2004  
 Last Updated on STN: 16 Sep 2004

ABSTRACT: Diabetes mellitus frequently leads to end-stage renal disease. Diabetic nephropathy develops in approximately 20% of patients with type 1 or type 2 diabetes mellitus after 20 years of diabetes mellitus duration. The correlation between anemia and chronic renal failure caused by diabetes mellitus has been well documented. Erythropoietin is most frequently used in patients receiving dialysis. The initial dose of intravenously administered erythropoietin for adults is 100-180 IU/kg body weight weekly, divided into 3 doses over the week. Hemoglobin (Hgb) and hematocrit (Htc) values should be measured at baseline and then every 2 weeks of treatment introduction as well as after any dose increment or reduction until the target and stable Hgb value is achieved and the erythropoietin maintenance dose determined. Subsequently, Hgb and Htc values should be determined every 4 weeks. All patients receive erythropoietin intravenously in doses from 2000 to 12000 IU weekly. Not all patients with chronic renal failure should be treated with erythropoietin, as 20% of patients on hemodialysis and 40% of those on peritoneal dialysis can maintain Hgb concentrations above 100 g/L and Htc above 0.30 with appropriate dialysis and dietary regimen and adequate iron stores. In patients receiving peritoneal dialysis it is not necessary to introduce erythropoietin therapy during the first 3 months of dialysis, because elevated Hgb concentrations (mean 10-20 g/L) can be expected in this initial period. Patients with chronic renal failure should have an adequate iron concentration (0.33) to achieve and maintain Hgb concentration at a minimum of 110 g/L. Erythropoietin can be administered subcutaneously, intravenously or intraperitoneally into 'dry abdomen', which should be left so for 6-8 hours. On intraperitoneal erythropoietin administration higher doses are required (by 15%-50%) than when it is administered subcutaneously or intravenously. Clinical usage of erythropoietin has not been defined in patients with type 2 diabetes mellitus and renal damage with anemia who have not yet developed end-stage renal disease.

CONTROLLED TERM: Medical Descriptors:

\*anemia: CO, complication  
\*anemia: DT, drug therapy  
chronic kidney failure: CO, complication  
chronic kidney failure: TH, therapy  
clinical trial  
comorbidity  
diet  
dose response  
drug dose reduction  
drug dose regimen  
drug megadose  
hematocrit  
hemodialysis  
hemoglobin determination  
human  
insulin dependent diabetes mellitus  
    iron blood level  
kidney failure: CO, complication  
kidney failure: TH, therapy  
    \*non insulin dependent diabetes mellitus  
peritoneal dialysis  
review

## CONTROLLED TERM:

## Drug Descriptors:

\*erythropoietin: CT, clinical trial  
\*erythropoietin: DO, drug dose  
\*erythropoietin: DT, drug therapy  
\*erythropoietin: IP, intraperitoneal drug administration  
\*erythropoietin: IV, intravenous drug administration  
\*erythropoietin: SC, subcutaneous drug administration  
hemoglobin: EC, endogenous compound

## CAS REGISTRY NO.:

(erythropoietin) 11096-26-7; (hemoglobin) 9008-02-0

## SEARCH HISTORY

=&gt; d his nofile

(FILE 'HOME' ENTERED AT 09:00:23 ON 30 JUL 2008)

FILE 'CAPLUS' ENTERED AT 09:00:37 ON 30 JUL 2008

E US2004-634477/APPS  
 E US2003-634477/APPS

L1 1 SEA ABB=ON US2003-634477/AP  
 D SCAN  
 SEL RN

FILE 'REGISTRY' ENTERED AT 09:03:35 ON 30 JUL 2008

L2 1 SEA ABB=ON 11096-26-7  
 L3 1 SEA ABB=ON 209810-58-2  
 L4 7 SEA ABB=ON (11096-26-7/B1 OR 113427-24-0/B1 OR 122312-54-3/B1  
 OR 209810-58-2/B1 OR 668496-68-2/B1 OR 668496-69-3/B1 OR  
 7439-89-6/B1)  
 L5 5 SEA ABB=ON L4 NOT (L2 OR L3)  
 D SCAN  
 D SCAN L3  
 D SCAN L2  
 L6 1 SEA ABB=ON 7439-89-6  
 E POLYETHYLENE GLYCOL/CN  
 L7 1 SEA ABB=ON POLYETHYLENE GLYCOL/CN

FILE 'CAPLUS' ENTERED AT 09:05:03 ON 30 JUL 2008

L8 448 SEA ABB=ON LEHMANN P?/AU  
 L9 9 SEA ABB=ON ROEDDINGER R?/AU  
 L10 2183 SEA ABB=ON WALTER MATSUI R?/AU OR WALTER R?/AU OR MATSUI  
 R?/AU  
 L11 12091 SEA ABB=ON L2  
 L12 441 SEA ABB=ON L2/D  
 L13 452 SEA ABB=ON L3  
 L14 472091 SEA ABB=ON L6  
 L15 108470 SEA ABB=ON L7  
 L16 35957 SEA ABB=ON PEG?/OBI  
 L17 38 SEA ABB=ON (L13 OR (L12 AND (L15 OR L16))). AND L14  
 L18 128446 SEA ABB=ON DIABET?/?/OBI  
 L19 4 SEA ABB=ON L17 AND L18  
 D SCAN TI  
 D SCAN  
 D SCAN L1  
 L20 29210 SEA ABB=ON GLYCOSYLAT?/?/OBI  
 L21 25 SEA ABB=ON (L11 AND (L16 OR L20)) AND L18  
 L22 991257 SEA ABB=ON IRON/OBI  
 L23 29660 SEA ABB=ON ANEMI?/?/OBI  
 L24 6854 SEA ABB=ON RETICULOCYT?/?/OBI  
 L25 14 SEA ABB=ON (L11 AND (L16 OR L20 OR L15)) AND L18 AND (L14 OR  
 L22 OR L23 OR L24)  
 D SCAN TI  
 L26 1 SEA ABB=ON DEGREE/TI AND L25  
 D SCAN  
 D QUE L25  
 L27 12741 SEA ABB=ON ERYTHROPOIETIN/OBI  
 L28 2577 SEA ABB=ON EPO/OBI  
 L29 403 SEA ABB=ON (L27 OR L28 OR L14) (L) (L16 OR L20 OR L15)  
 L30 14 SEA ABB=ON L29 AND L18  
 D QUE

L31           8 SEA ABB=ON L29 AND L18 AND (L22 OR L23 OR L24 OR L14)  
 L32           12 SEA ABB=ON (L27 OR L28 OR L11) (L) (L16 OR L14 OR L20) AND L18  
               AND (L22 OR L23 OR L24 OR L14)  
               D SCAN TI HITIND  
               D QUE  
               D QUE L14  
               D QUE L13  
               D QUE L12  
 L33           4 SEA ABB=ON (L27 OR L28 OR L11) (L) (L15 OR L16 OR L20) AND L18  
               AND (L22 OR L23 OR L24 OR L14)  
               D SCAN TI  
               D SCAN TI L19  
 L34           8 SEA ABB=ON L13 AND L18 AND (L22 OR L23 OR L24 OR L14)  
 L35           6 SEA ABB=ON L34 NOT L33  
               D SCAN TI  
 L36           4 SEA ABB=ON L33 OR (L33 AND L13)  
 L37           3 SEA ABB=ON (L1 OR L8 OR L9 OR L10) AND ((L12 OR L13) OR (L11  
               AND (L15 OR L16 OR L20)))

FILE 'WPIX' ENTERED AT 09:33:04 ON 30 JUL 2008

L38           882 SEA ABB=ON WALTER MATSUI R?/AU OR WALTER R?/AU OR MATSUI  
               R?/AU  
 L39           7 SEA ABB=ON ROEDDINGER R?/AU  
 L40           190 SEA ABB=ON LEHMANN P?/AU  
 L41           3 SEA ABB=ON L38 AND L39 AND L40  
               D TRIAL 1-3  
 L42           2477 SEA ABB=ON ERYTHROPOIETIN/BI, ABEX  
 L43           1121 SEA ABB=ON EPO/BI, ABEX  
 L44           12 SEA ABB=ON DARBEPOIETIN/BI, ABEX  
 L45           49879 SEA ABB=ON DIABET?/BI, ABEX  
 L46           30843 SEA ABB=ON PEG?/BI, ABEX  
 L47           51402 SEA ABB=ON POLYETHYLENEGLYCOL/BI, ABEX OR POLY/BI, ABEX (W) (ETHYL  
               ENE GLYCOL/BI, ABEX OR ETHYLENE GLYCOL/BI, ABEX) OR POLYETHYLENE  
               GLYCOL/BI, ABEX  
 L48           4420 SEA ABB=ON GLYCOSYLAT?/BI, ABEX  
 L49           78 SEA ABB=ON (L42 OR L43) AND L45 AND (L46 OR L47 OR L48)  
 L50           0 SEA ABB=ON L44 AND L45 AND (L46 OR L47 OR L48)  
 L51           7 SEA ABB=ON L44 AND (L45 OR L46 OR L47 OR L48)  
               D SCAN  
 L52           10 SEA ABB=ON (L42 OR L43) (8A) (L46 OR L47 OR L48) AND L45  
 L53           264038 SEA ABB=ON IRON/BI, ABEX  
 L54           6529 SEA ABB=ON ANEMI?/BI, ABEX  
 L55           494 SEA ABB=ON RETICULOCYT?/BI, ABEX  
 L56           26 SEA ABB=ON HEMOSIDERO?/BI, ABEX  
 L57           303 SEA ABB=ON HEMOCHROMATO?/BI, ABEX  
 L58           29 SEA ABB=ON HAEMOSIDERO?/BI, ABEX  
 L59           81 SEA ABB=ON HAEMOCHROMATO?/BI, ABEX  
               D QUE L52  
 L60           30 SEA ABB=ON L49 AND (L53 OR L54 OR L55 OR L56 OR L57 OR L58 OR  
               L59)  
 L61           20 SEA ABB=ON (L42 OR L43) (S) (L46 OR L47 OR L48) AND L45 AND  
               (L53 OR L54 OR L55 OR L56 OR L57 OR L58 OR L59)  
 L62           4 SEA ABB=ON (L42 OR L43) (8A) (L46 OR L47 OR L48) AND L45 AND  
               (L53 OR L54 OR L55 OR L56 OR L57 OR L58 OR L59)  
               D SCAN  
 L63           545 SEA ABB=ON L53 (3A) DISTRIBUT?/BI, ABEX  
 L64           5 SEA ABB=ON (L42 OR L43 OR L44) AND L63  
               D SCAN  
 L65           913 SEA ABB=ON L53 (3A) (STOR?/BI, ABEX OR METABOLI?/BI, ABEX)  
 L66           13 SEA ABB=ON (L42 OR L43 OR L44) AND L65

L67           12 SEA ABB=ON L66 NOT (L41 OR L62 OR L64)  
               D SCAN  
 L68           30878 SEA ABB=ON OVERLOAD?/BI, ABEX  
 L69           4 SEA ABB=ON (L42 OR L43 OR L44) AND L65 AND L68  
               D SCAN  
 L70           2 SEA ABB=ON (L42 OR L43 OR L44) AND L65 AND L68 NOT ANTIBOD?/BI  
               ,ABEX  
               D SCAN

FILE 'MEDLINE' ENTERED AT 09:47:09 ON 30 JUL 2008

L71           1077 SEA ABB=ON WALTER MATSUI R?/AU OR WALTER R?/AU OR MATSUI  
               R?/AU  
 L72           0 SEA ABB=ON ROEDDINGER R?/AU  
 L73           382 SEA ABB=ON LEHMANN P?/AU  
 L74           13344 SEA ABB=ON IRON METABOLISM DISORDERS+NT/CT  
 L75           16537 SEA ABB=ON ERYTHROPOIETIN+NT/CT  
 L76           49008 SEA ABB=ON DIABETES MELLITUS, TYPE 2+NT/CT  
 L77           2 SEA ABB=ON L74 AND L75 AND L76  
               D TRIAL 1-2  
 L78           9965 SEA ABB=ON IRON/CT(L) BL/CT  
 L79           3 SEA ABB=ON L75 AND L76 AND L78  
               D TRIAL 1-3  
 L80           10150 SEA ABB=ON L75(L) (AD OR TU OR PD OR PK)/CT  
 L81           1 SEA ABB=ON L80 AND L76 AND (L78 OR L74)

FILE 'STNGUIDE' ENTERED AT 09:51:17 ON 30 JUL 2008

FILE 'EMBASE' ENTERED AT 10:06:48 ON 30 JUL 2008

FILE 'MEDLINE' ENTERED AT 10:07:13 ON 30 JUL 2008  
 L82           0 SEA ABB=ON (L71 OR L72 OR L73) AND L75  
 FILE 'MEDLINE' ENTERED AT 10:07:33 ON 30 JUL 2008  
 L83           0 SEA ABB=ON (L71 OR L72 OR L73) AND (L75 OR L74 OR L78)

FILE 'EMBASE' ENTERED AT 10:08:02 ON 30 JUL 2008  
 L84           797 SEA ABB=ON WALTER MATSUI R?/AU OR WALTER R?/AU OR MATSUI  
               R?/AU  
 L85           0 SEA ABB=ON ROEDDINGER R?/AU  
 L86           417 SEA ABB=ON LEHMANN P?/AU  
               E DIABETES MELLITUS, TYPE 2+ALL/CT  
 L87           53891 SEA ABB=ON NON INSULIN DEPENDENT DIABETES MELLITUS/CT  
               E ERYTHROPOIETIN/CT  
               E ERYTHROPOIETIN AN/CT  
               E ERYTHROPOIETIN DER/CT  
               E ERYTHROPOIETIN/CT  
               E E3+ALL  
 L88           15072 SEA ABB=ON ERYTHROPOIETIN/CT OR ERYTHROPOIETIN DERIVATIVE/CT  
               E IRON METABOLISM DISORDERS+ALL/CT  
               E E2+ALL  
 L89           7342 SEA ABB=ON IRON METABOLISM DISORDER+NT/CT  
               E BLOOD IRON/CT  
               E E3+ALL  
               E E2+ALL  
 L90           3643 SEA ABB=ON IRON BLOOD LEVEL/CT  
 L91           1 SEA ABB=ON (L84 OR L85 OR L86) AND (L88 OR L89 OR L90)  
               D TRIAL  
 L92           1 SEA ABB=ON L87 AND L88 AND (L89 OR L90)  
               D TRIAL

FILE 'STNGUIDE' ENTERED AT 10:13:30 ON 30 JUL 2008

FILE 'CAPLUS' ENTERED AT 10:14:07 ON 30 JUL 2008  
D QUE L37

FILE 'WPIX' ENTERED AT 10:14:08 ON 30 JUL 2008  
D QUE L41

FILE 'MEDLINE' ENTERED AT 10:14:08 ON 30 JUL 2008  
D QUE L83

FILE 'EMBASE' ENTERED AT 10:14:08 ON 30 JUL 2008  
D QUE L91

FILE 'CAPLUS, WPIX, EMBASE' ENTERED AT 10:14:09 ON 30 JUL 2008  
L93 4 DUP REM L37 L41 L91 (3 DUPLICATES REMOVED)  
ANSWERS '1-3' FROM FILE CAPLUS  
ANSWER '4' FROM FILE EMBASE  
D IBIB AB HITIND 1-3  
D IALL 4

FILE 'MEDLINE' ENTERED AT 10:14:30 ON 30 JUL 2008  
D QUE L81

FILE 'EMBASE' ENTERED AT 10:15:03 ON 30 JUL 2008  
D QUE L92

FILE 'CAPLUS' ENTERED AT 10:15:03 ON 30 JUL 2008  
D QUE L36  
L94 3 SEA ABB=ON L36 NOT L37

FILE 'WPIX' ENTERED AT 10:15:03 ON 30 JUL 2008  
D QUE L62  
D QUE L64  
D QUE L70  
L95 7 SEA ABB=ON (L62 OR L64 OR L70) NOT L41

FILE 'STNGUIDE' ENTERED AT 10:15:09 ON 30 JUL 2008

FILE 'MEDLINE, CAPLUS, WPIX, EMBASE' ENTERED AT 10:15:25 ON 30 JUL 2008  
L96 12 DUP REM L81 L94 L95 L92 (0 DUPLICATES REMOVED)  
ANSWER '1' FROM FILE MEDLINE  
ANSWERS '2-4' FROM FILE CAPLUS  
ANSWERS '5-11' FROM FILE WPIX  
ANSWER '12' FROM FILE EMBASE  
D IALL 1  
D IBIB AB HITIND 2-4  
D IALL ABEX TECH 5-11  
D IALL 12

=>

11/013,5760  
11/013,5760

STRUCTURE SEARCH

=> fil reg; d stat que l105; fil capl; d que nos l106  
FILE 'REGISTRY' ENTERED AT 11:04:24 ON 30 JUL 2008  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 JUL 2008 HIGHEST RN 1036977-72-6  
DICTIONARY FILE UPDATES: 29 JUL 2008 HIGHEST RN 1036977-72-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

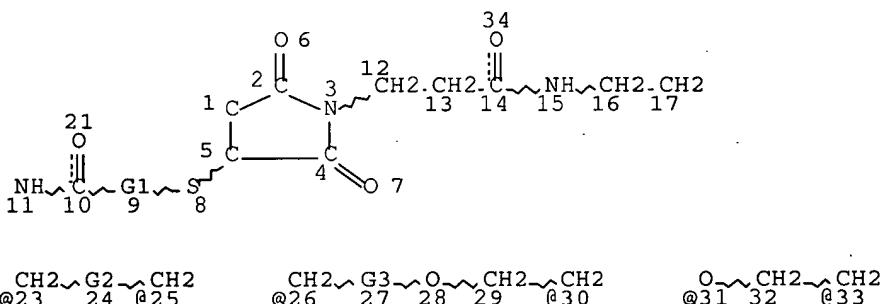
TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

L102 STR



VAR G1=CH2/23-10 25-8/26-10 30-8

REP G2=(0-8) CH2

REP G3=(0-9) 31-26 33-28

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

L105 25 SEA FILE=REGISTRY SSS FUL L102

100.0% PROCESSED 180 ITERATIONS  
SEARCH TIME: 00.00.01

25 ANSWERS

FILE 'CAPLUS' ENTERED AT 11:04:24 ON 30 JUL 2008  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
 COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 30 Jul 2008 VOL 149 ISS 5  
 FILE LAST UPDATED: 29 Jul 2008 (20080729/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>  
 'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L102 STR  
 L105 25 SEA FILE=REGISTRY SSS FUL L102  
 L106 11 SEA FILE=CAPLUS ABB=ON L105

=> d ibib abs hitstr l106 1-11; fil hom

L106 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2008:799491 CAPLUS Full-text  
 TITLE: Preparation of paramagnetic nanoparticles conjugated to leukotriene b4 (LTB4) receptor antagonists, and their use as MRI contrast agents for the detection of infection and inflammation  
 INVENTOR(S): Harris, Thomas D.  
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Pharma Company, USA  
 SOURCE: PCT Int. Appl., 39pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008079834	A2	20080703	WO 2007-US88025	20071219
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI,			

GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,  
 KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,  
 MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,  
 PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,  
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW  
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
 IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,  
 GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,  
 BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2006-871154P P 20061221

AB Nanoparticle-based compns. and emulsions that are specifically targeted to leukotriene B4 (LTB4) receptors, and employing LTB4 receptor antagonist targeting agents, are set forth. In addition, there is provided the use of non-antibody based compns. for such targeting. The compns. of the invention are useful as imaging agents in diagnostic and therapeutic applications.

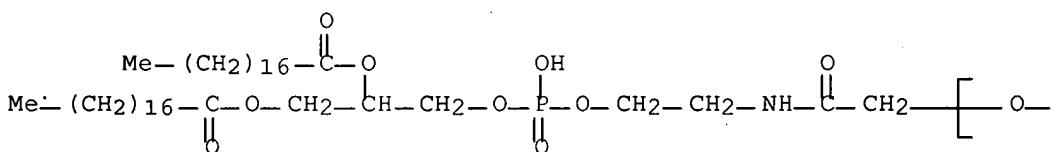
IT 1035928-13-2P

RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of paramagnetic nanoparticles conjugated to leukotriene B4 (LTB4) receptor antagonists; and their use as MRI contrast agents for the detection of infection and inflammation)

RN 1035928-13-2 CAPLUS

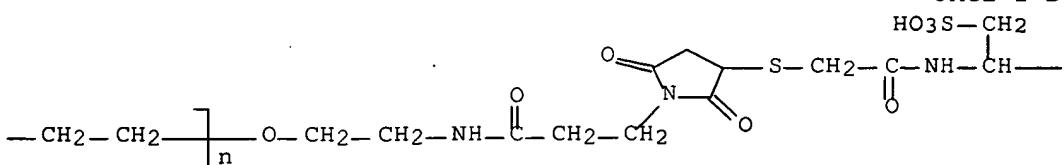
CN INDEX NAME NOT YET ASSIGNED

PAGE 1-A

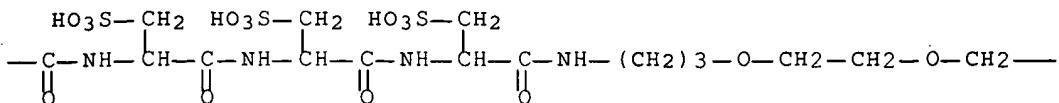


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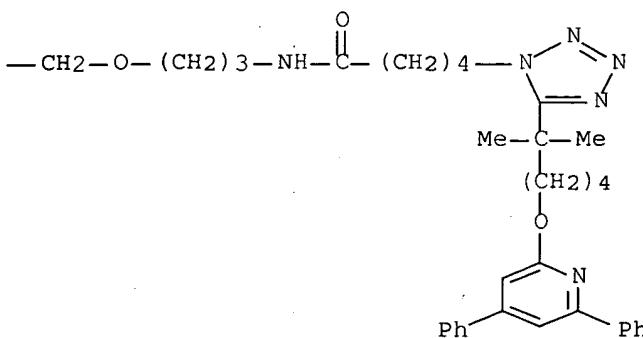
PAGE 1-B



PAGE 1-C



PAGE 1-D



L106 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2008:700214 CAPLUS Full-text  
 DOCUMENT NUMBER: 149:62716  
 TITLE: Compositions and methods for imaging tumor neovasculature employing chelated radioisotopes  
 INVENTOR(S): Lanza, Gregory M.  
 PATENT ASSIGNEE(S): Barnes-Jewish Hospital, USA  
 SOURCE: PCT Int. Appl., 34pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008070464	A2	20080612	WO 2007-US85446	20071121
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2006-860546P P 20061121  
 OTHER SOURCE(S): MARPAT 149:62716

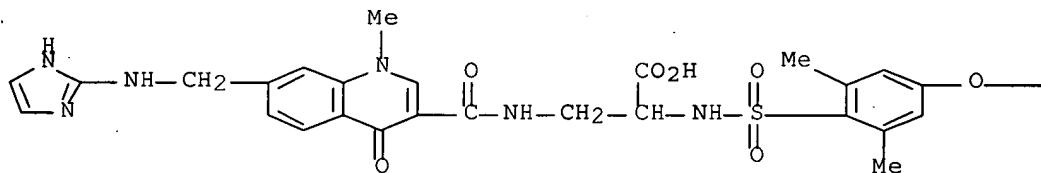
AB Methods to image neovasculature associated with tumors using emulsions of targeted lipid/surfactant-coated nanoparticles coupled to chelating agents containing radioisotopes are described. Thus, the emulsified perfluoroctyl bromide (PFOB) nanoparticles were prepared comprising 20% volume/volume of PFOB, 2% weight/volume of a surfactant, and water for the balance. The surfactant co-mixture for the  $\alpha\beta 3$  integrin-targeted particles included 3-5 mol% bis(pyridyl)-lysine-caproyl-phosphatidylethanolamine, 0.1 mol% vitronectin antagonist complexed to PEG2000-phosphatidylethanolamine (preparation given), and egg phosphatidylcholine for balance. The nanoparticles were radiolabeled with  $^{99m}\text{Tc}$  and used for SPECT/CT imaging in a rabbit VX-2 carcinoma tumor model.

IT 1032007-96-7P  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (comps. and methods for imaging tumor neovasculature employing chelating agents containing radioisotopes)

RN 1032007-96-7 CAPLUS

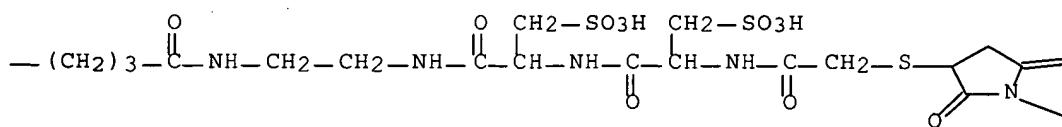
CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[2-[3-[3-[[[(4S,7S)-16-[4-[[[(1S)-1-carboxy-2-[[[1,4-dihydro-6-[(1H-imidazol-2-ylamino)methyl]-1-methyl-4-oxo-3-quinolinyl]carbonyl]amino]ethyl]amino]sulfonyl]-3,5-dimethylphenoxy]-2,5,8,13-tetraoxo-4,7-bis(sulfomethyl)-3,6,9,12-tetraazahexadec-1-yl]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]ethyl]- $\omega$ -[(10R)-7-hydroxy-7-oxido-2,13-dioxo-10-[(1-oxooctadecyl)oxy]-6,8,12-trioxa-3-aza-7-phosphatriacont-1-yl]oxy]-, sodium salt (1:1) (CA INDEX NAME)

PAGE 1-A

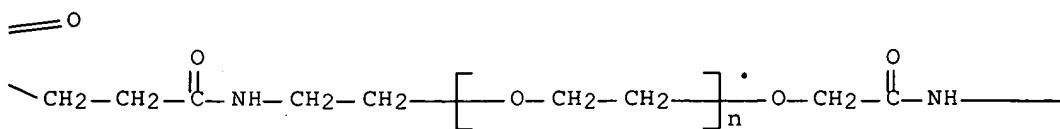


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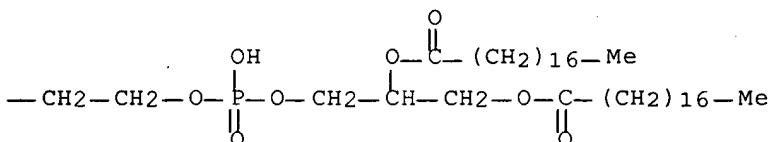
PAGE 1-B



PAGE 1-C



PAGE 1-D



L106 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2008:588877 CAPLUS Full-text  
 DOCUMENT NUMBER: 148:556983  
 TITLE: Detection of mass-tagged biomolecules by matrix-free desorption-ionization mass spectrometry  
 INVENTOR(S): Chaurand, Pierre; Norris, Jeremy L.; Porter, Ned A.; Yang, Junhai; Caprioli, Richard M.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 32pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080113875	A1	20080515	US 2007-852114	20070907
PRIORITY APPLN. INFO.:			US 2006-825014P	P 20060908

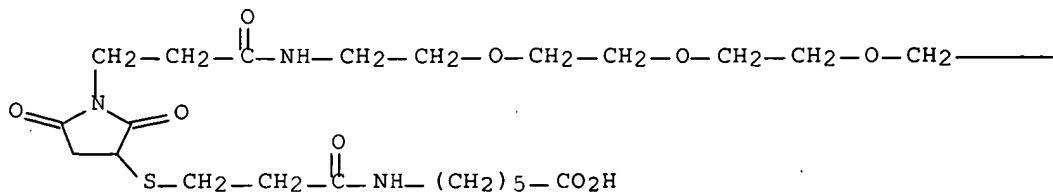
AB The present invention provides methods for obtaining information of a plurality of target mols. by matrix-free LDI (laser desorption/ionization)-MS. Mass tagged complexes for detection of target mols. comprise a target mol. binding domain, and a mass tag separated by a cleavable linker. Methods of the invention may be used for example to analyze the distribution of a multiple target mols., such as biomols. or drugs, in a complex sample, such as a tissue section. In particular, the method is used for detection of mass-tagged antibodies, such as antibodies labeled by mass-tagged dendrimers.

IT 1025680-58-3DP, conjugates with dendrimers and antibodies  
 RL: ANT (Analyte); SPN (Synthetic preparation); ANST (Analytical study);  
 PREP (Preparation)  
 (detection of mass-tagged biomols. by matrix-free desorption-ionization mass spectrometry)

RN 1025680-58-3 CAPLUS

CN 4,7,10,13-Tetraoxa-16-azanonadecanoic acid, 19-[3-[[3-[(5-carboxypentyl)amino]-3-oxopropyl]thio]-2,5-dioxo-1-pyrrolidinyl]-17-oxo-(CA INDEX NAME)

PAGE 1-A



PAGE 1-B

 $-\text{CH}_2-\overset{\text{O}}{\underset{\parallel}{\text{C}}}-\text{CH}_2-\text{CH}_2-\text{CO}_2\text{H}$ 

L106 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2008:318097 CAPLUS Full-text  
 DOCUMENT NUMBER: 148:347309  
 TITLE: Compounds as aptamer-dimers and their uses in diagnosis and therapy  
 INVENTOR(S): Friebe, Matthias; Stephens, Andrew; Srinivasan, Ananth; Hecht, Maren  
 PATENT ASSIGNEE(S): Bayer Schering Pharma Aktiengesellschaft, Germany  
 SOURCE: PCT Int. Appl., 65pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008028530	A1	20080313	WO 2007-EP5875	20070703
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1897886	A1	20080312	EP 2006-90164	20060908
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: EP 2006-90164 A 20060908

OTHER SOURCE(S): MARPAT 148:347309

AB The object of the present invention is solved by compns. of peptide linkers and their use for synthesis and annealing of aptamer oligonucleotides in form of dimers. The present invention in particularly provides said compns. for

the use as a diagnostic and/or therapeutic agent. In another preferred embodiment the present invention relates to a kit for preparing a radio pharmaceutical preparation, said kit comprising a vial comprising a quantity of the compound according to the invention. A further preferred embodiment of the present invention relates to methods of producing said compds., comprising synthesis of said compound in an automated peptide synthesizer. In another preferred embodiment the present invention concerns the use of said compds. according to the present invention for the manufacture of a medicament, preferably for diagnosis or therapy of proliferative diseases. In a further preferred embodiment the present invention concerns methods for treating or diagnosing patients administering or utilizing the compds. according to the present invention.

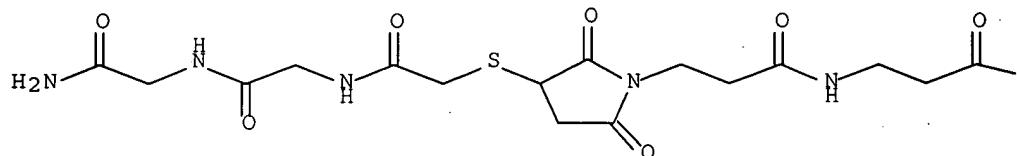
IT 1013020-66-0DP, 99mTc labeled tenascin C aptamer dimer conjugates  
 1013020-67-1DP, 99mTc labeled tenascin C aptamer dimer conjugates  
 1013020-68-2DP, 99mTc labeled tenascin C aptamer dimer conjugates  
 1013020-69-3DP, 99mTc labeled tenascin C aptamer dimer conjugates  
 1013020-70-6DP, 99mTc labeled tenascin C aptamer dimer conjugates  
 1013020-71-7DP, 99mTc labeled tenascin C aptamer dimer conjugates  
 1013020-72-8DP, 99mTc labeled tenascin C aptamer dimer conjugates  
 RL: DGN (Diagnostic use); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (compds. as aptamer-dimers and their uses in diagnosis and therapy)

RN 1013020-66-0 CAPLUS

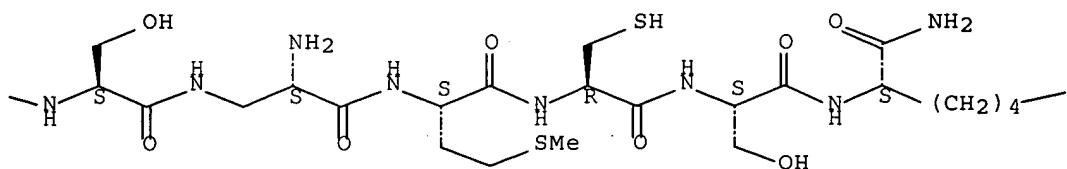
CN L-Lysinamide, N-[3-(3-mercaptop-2,5-dioxo-1-pyrrolidinyl)-1-oxopropyl]- $\beta$ -alanyl-L-seryl-(2S)-2-amino- $\beta$ -alanyl-L-methionyl-L-cysteinyl-L-seryl-N6-[3-(3-mercaptop-2,5-dioxo-1-pyrrolidinyl)-1-oxopropyl]-(1 $\rightarrow$ 1'), (7 $\rightarrow$ 1'')-bis(thioether) with N-(2-mercaptopacetyl)glycylglycinamide (CA INDEX NAME)

Absolute stereochemistry.

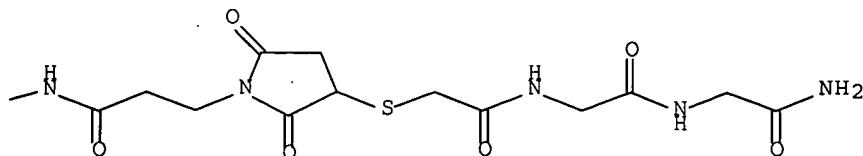
PAGE 1-A



PAGE 1-B



PAGE 1-C

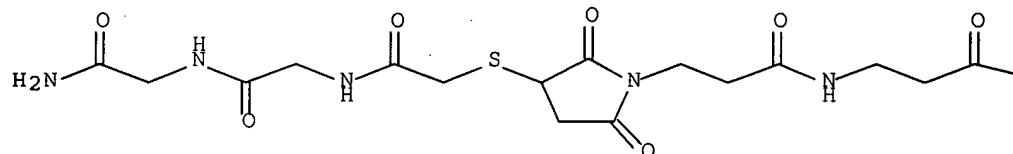


RN 1013020-67-1 CAPLUS

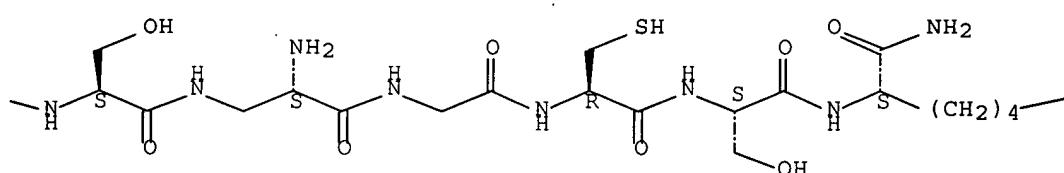
CN L-Lysinamide, N-[3-(3-mercaptop-2,5-dioxo-1-pyrrolidinyl)-1-oxopropyl]-  
 β-alanyl-L-seryl-(2S)-2-amino-β-alanylglycyl-L-cysteinyl-L-seryl-  
 N6-[3-(3-mercaptop-2,5-dioxo-1-pyrrolidinyl)-1-oxopropyl]-,  
 (1→1'), (7→1'')-bis(thioether) with N-(2-  
 mercaptoacetyl)glycylglycinamide (CA INDEX NAME)

Absolute stereochemistry.

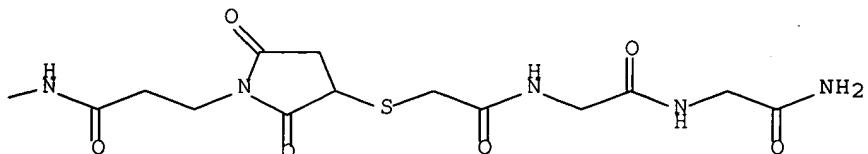
PAGE 1-A



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PAGE 1-C

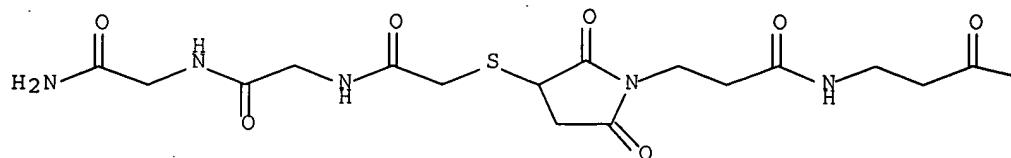


RN 1013020-68-2 CAPLUS

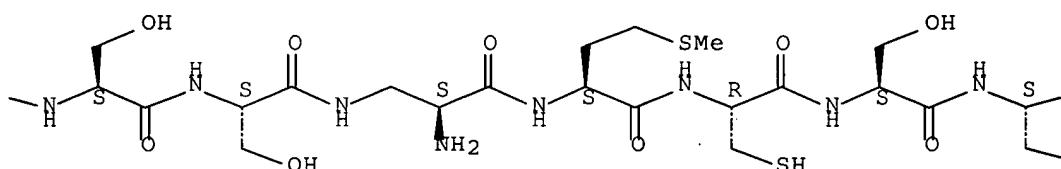
CN L-Lysinamide, N-[3-(3-mercaptop-2,5-dioxo-1-pyrrolidinyl)-1-oxopropyl]-  
 β-alanyl-L-seryl-L-seryl-(2S)-2-amino-β-alanyl-L-methionyl-L-  
 cysteinyl-L-seryl-L-seryl-N6-[3-(3-mercaptop-2,5-dioxo-1-pyrrolidinyl)-1-  
 oxopropyl]-, (1→1'), (9→1'')-bis(thioether) with  
 N-(2-mercaptopacetyl)glycylglycinamide (CA INDEX NAME)

Absolute stereochemistry.

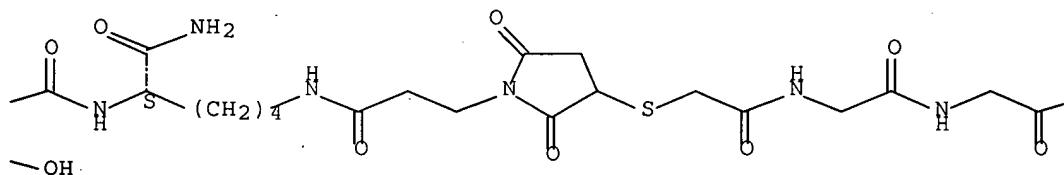
PAGE 1-A



PAGE 1-B



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PAGE 1-D

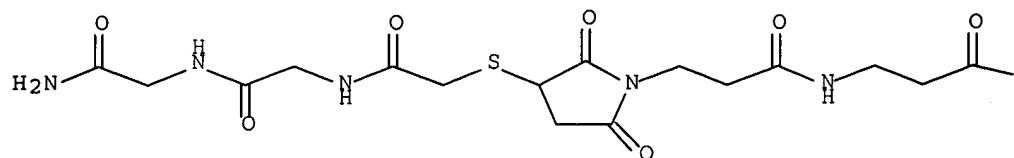
NH<sub>2</sub>

RN 1013020-69-3 CAPLUS

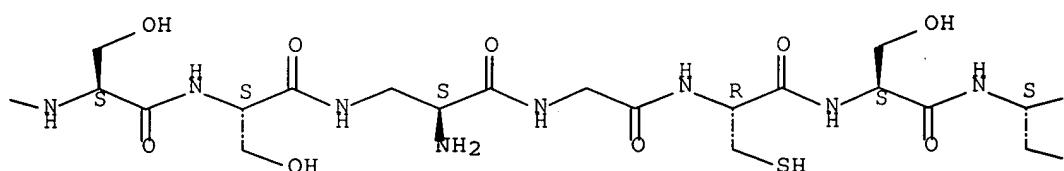
CN L-Lysinamide, N-[3-(3-mercaptop-2,5-dioxo-1-pyrrolidinyl)-1-oxopropyl]-  
 β-alanyl-L-seryl-L-seryl-(2S)-2-amino-β-alanylglycyl-L-cysteinyl-  
 L-seryl-L-seryl-N6-[3-(3-mercaptop-2,5-dioxo-1-pyrrolidinyl)-1-oxopropyl]-,  
 (1→1'), (9→1'')-bis(thioether) with N-(2-  
 mercaptoacetyl)glycylglycinamide (CA INDEX NAME)

Absolute stereochemistry.

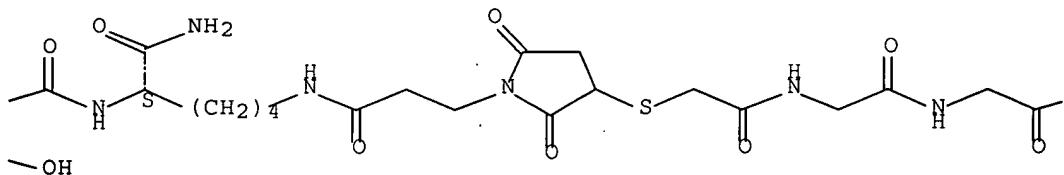
PAGE 1-A



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PAGE 1 - D

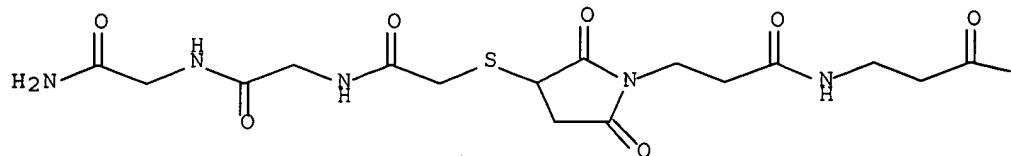
$\text{NH}_2$

RN 1013020-70-6 CAPLUS

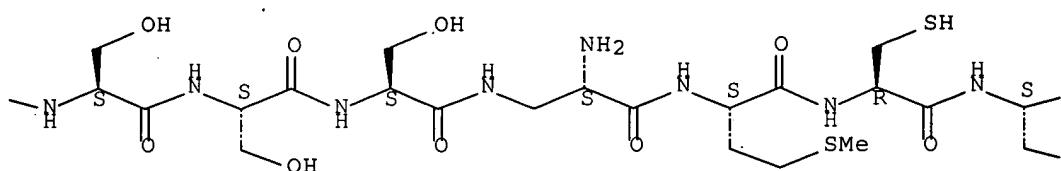
CN L-Lysinamide, N-[3-(3-mercaptopropanoyl)-1-oxopropyl]-  
β-alanyl-L-seryl-L-seryl-L-seryl-(2S)-2-amino-β-alanyl-L-  
methionyl-L-cysteinyl-L-seryl-L-seryl-L-seryl-N6-[3-(3-mercaptopropanoyl)-1-oxopropyl]-, (1→1'), (11→1'')-  
bis(thioether) with N-(2-mercaptopropanoyl)glycylglycinamide (CA INDEX NAME)

## Absolute stereochemistry.

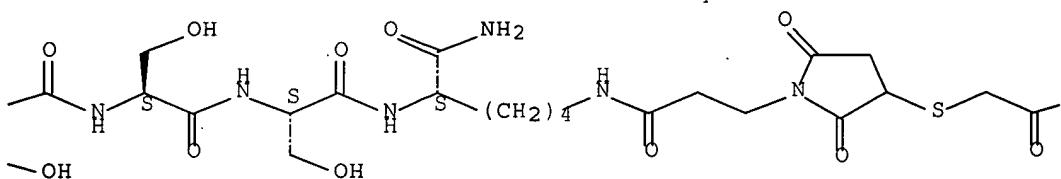
PAGE 1 - A



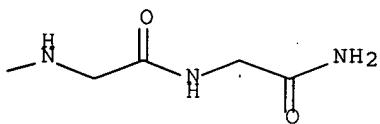
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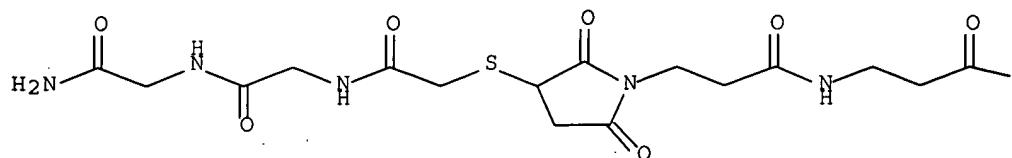


RN 1013020-71-7 CAPLUS

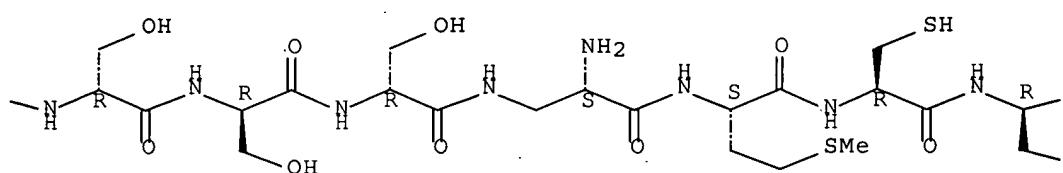
CN L-Lysinamide, N-[3-(3-mercaptopropanoyl)-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]-  
β-alanyl-D-seryl-D-seryl-D-seryl-(2S)-2-amino-β-alanyl-L-methionyl-L-cysteinyl-D-seryl-D-seryl-D-seryl-N6-[3-(3-mercaptopropanoyl)-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]-, (1→1'), (11→1'')-bis(thioether) with N-(2-mercaptopropanoyl)glycylglycinamide (CA INDEX NAME)

## Absolute stereochemistry.

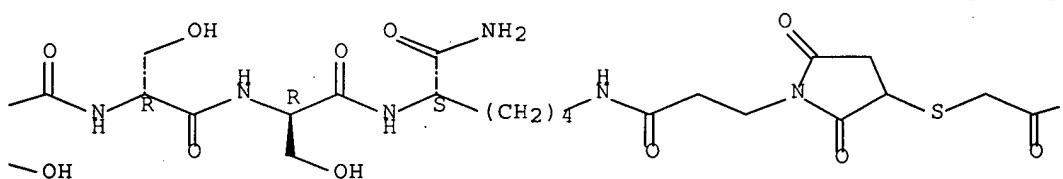
PAGE 1-A



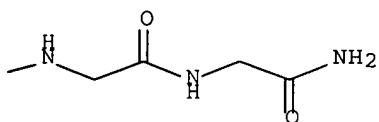
PAGE 1-B



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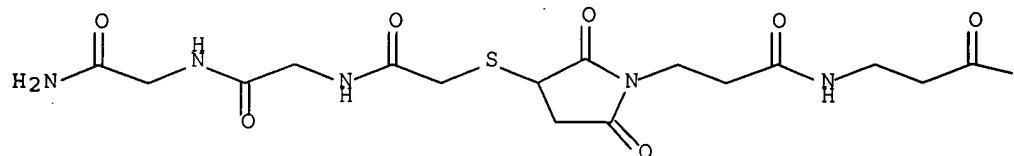


RN 1013020-72-8 CAPLUS

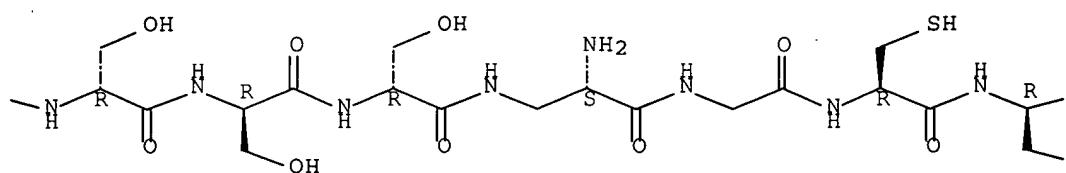
CN L-Lysinamide, N-[3-(3-mercaptop-2,5-dioxo-1-pyrrolidinyl)-1-oxopropyl]-  
 β-alanyl-D-seryl-D-seryl-D-seryl-(2S)-2-amino-β-alanylglycyl-L-  
 cysteinyl-D-seryl-D-seryl-D-seryl-N6-[3-(3-mercaptop-2,5-dioxo-1-  
 pyrrolidinyl)-1-oxopropyl]-, (1→1'), (11→1'')-bis(thioether)  
 with N-(2-mercaptopacetyl)glycylglycinamide (CA INDEX NAME)

Absolute stereochemistry.

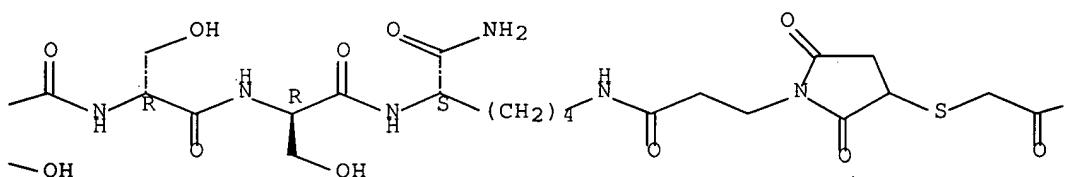
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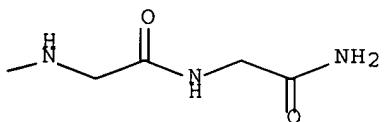
PAGE 1-B



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L106 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2006:153122 CAPLUS Full-text  
 DOCUMENT NUMBER: 145:263795  
 TITLE: Imaging chemically modified adenovirus for targeting tumors expressing integrin  $\alpha v\beta 3$  in living mice with mutant herpes simplex virus type 1 thymidine kinase PET reporter gene  
 AUTHOR(S): Xiong, Zhengming; Cheng, Zhen; Zhang, Xianzhong; Patel, Manish; Wu, Joseph C.; Gambhir, Sanjiv S.; Chen, Xiaoyuan  
 CORPORATE SOURCE: Molecular Imaging Program at Stanford (MIPS), Departments of Radiology and Bioengineering, Bio-X Program, Stanford University School of Medicine,

SOURCE: Stanford, CA, USA  
 Journal of Nuclear Medicine (2006), 47(1), 130-139  
 CODEN: JNMEAQ; ISSN: 0161-5505

PUBLISHER: Society of Nuclear Medicine  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

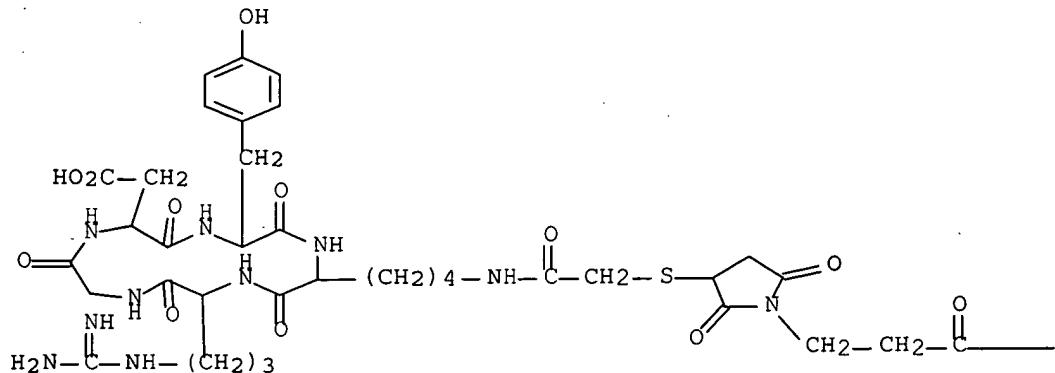
AB The aim of this study was to change adenovirus tropism by chemical modification of the fiber knobs with PEGylated RGD peptide for targeting integrin  $\alpha v\beta 3$  that is uniquely or highly expressed in tumor cells and neovasculature of tumors of various origins. Methods: The first generation Ad vector, which expresses the herpes simplex virus type 1 mutant thymidine kinase (HSV1-sr39tk) gene under the control of cytomegalovirus (CMV) promoter was conjugated with poly(ethylene glycol) (PEG) or RGD-PEG. The transduction efficiency of Ads (Adtk, PEG-Adtk, and RGD-PEG-Adtk) into different types of cells (293T, MCF7, MDA-MB-435, and U87MG) was analyzed and quantified by thymidine kinase (TK) assay using  $8-3^H$ -penciclovir ( $8-3^H$ -PCV) as substrate. The *in vivo* infectivity of the Ad vectors after i.v. administration into integrin  $\alpha v\beta 3$ -pos. U87MG and MDA-MB-435 tumor-bearing athymic nude mice was measured by both noninvasive microPET using  $9-[4-18^F$ -fluoro-3-(hydroxymethyl)butyl]guanine ( $18^F$ -FHBG) as a reporter probe and *ex vivo* TK assay of the tumor and tissue homogenates. Results: PEGylation completely abrogated coxsackievirus and adenovirus receptor (CAR)-knob interaction and the infectivity of PEG-Adtk is significantly lower than that of unmodified Adtk in CAR-pos. cells. RGD-PEG-modified virus (RGD-PEG-Adtk) had significantly higher infectivity than PEG-Adtk and the extent of increase is related to both CAR and integrin  $\alpha v\beta 3$  expression levels.  $18^F$ -FHBG had minimal nonspecific uptake in the liver and tumors that are void of sr39tk. Mice preinjected i.v. with unmodified Adtk resulted in high hepatic uptake and moderate tumor accumulation of the tracer. In contrast, RGD-PEG-Adtk administration resulted in significantly lower liver uptake without compromising the tumor accumulation of  $18^F$ -FHBG. Expression of TK in the liver and tumor homogenates corroborated with the magnitude of  $18^F$ -FHBG uptake quantified by noninvasive microPET. Anal. of liver and tumor tissue integrin level confirmed that RGD-integrin interaction is responsible for the enhanced tumor infectivity of RGD-PEG-Adtk. Conclusion: The results of this study suggest that RGD-PEG conjugation is an effective way to modify Ad vector tropism for improved systemic gene delivery. Noninvasive PET and  $18^F$ -FHBG are able to monitor *in vivo* transfectivity of both Adtk and RGD-PEG-Adtk vectors in the liver and tumors after i.v. injection.

IT 906802-69-5D, conjugates with adenovirus  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (imaging chemical modified adenovirus for targeting tumors expressing  
 integrin  $\alpha v\beta 3$  in living mice with mutant herpes simplex  
 virus type 1 thymidine kinase PET reporter gene)

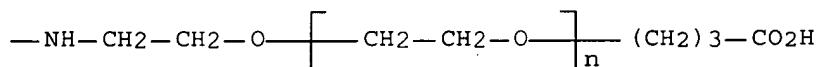
RN 906802-69-5 CAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -(3-carboxypropyl)- $\omega$ -hydroxy-,  
 5-ether with cyclo[L-arginylglycyl-L- $\alpha$ -aspartyl-D-tyrosyl-N6-[[[1-[3-  
 [(2-hydroxyethyl)amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]thio]acetyl]-  
 L-lysyl] (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L106 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2006:31256 CAPLUS Full-text  
 DOCUMENT NUMBER: 144:135221  
 TITLE: Polymeric prodrug hydrogel depo formulation for peptides, proteins, and nucleotides  
 INVENTOR(S): Hersel, Ulrich; Rau, Harald; Schnepf, Robert; Vetter, Dirk; Wegge, Thomas  
 PATENT ASSIGNEE(S): Complex Biosystems GmbH, Germany  
 SOURCE: PCT Int. Appl., 59 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006003014	A2	20060112	WO 2005-EP7316	20050705
WO 2006003014	A3	20070111		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,			

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,  
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,  
 LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,  
 NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,  
 SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,  
 ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,  
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM

EP 1625856 A1 20060215 EP 2004-19303 20040813  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR  
 EP 1781335 A2 20070509 EP 2005-767518 20050705  
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
 IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,  
 BA, HR, MK, YU

PRIORITY APPLN. INFO.: GB 2004-15041 A 20040705  
 EP 2004-19303 A 20040813  
 GB 2005-5250 A 20050315  
 WO 2005-EP7316 W 20050705

AB The application relates to a polymeric prodrug which comprises a hydrogel, a biol. active moiety and a reversible prodrug linker. The prodrug linker covalently links the hydrogel and the biol. active moiety at a position and the hydrogel has a plurality of pores with openings on the surface of the hydrogel. The diameter of the pores is larger than that of the biol. active moiety at least at all points of the pore between at least one of the openings and the position of the biol. active moiety. Thus, a maleimide-derivatized polyethylene glycol acrylamide meso porous hydrogel was prepared. The release of rh-insulin in vitro and in vivo from the hydrogel prodrug was studied.

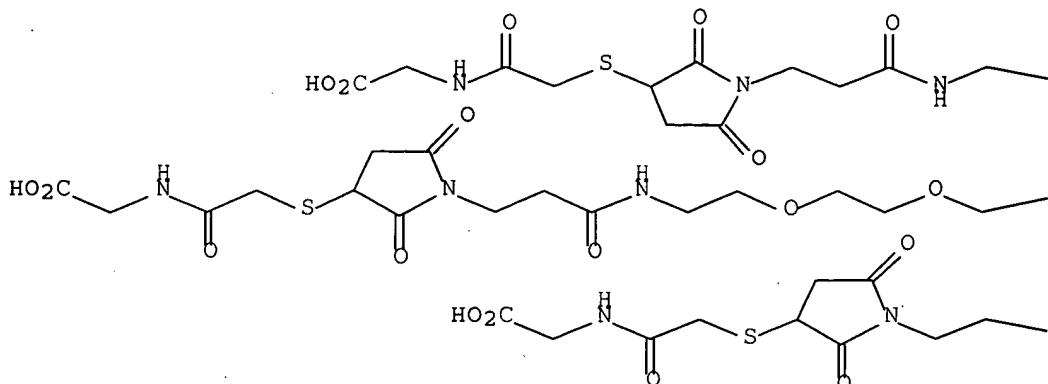
IT 873295-55-7P  
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
 (polymeric prodrug hydrogel depo formulation for peptides, proteins,  
 and nucleotides)

RN 873295-55-7 CAPLUS

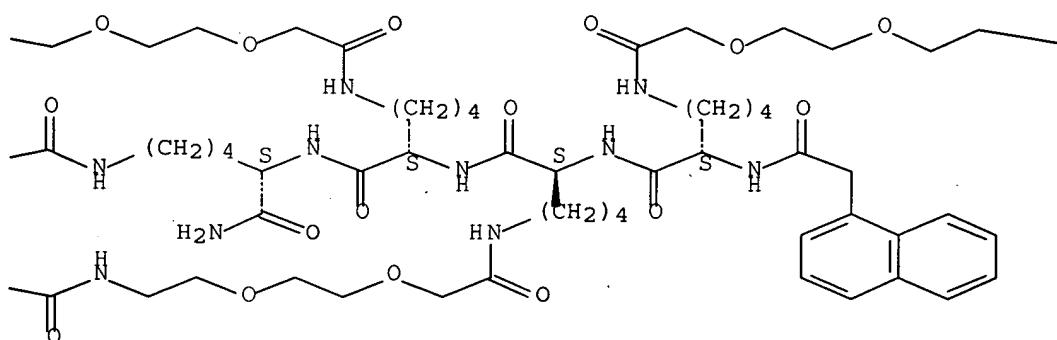
CN L-Lysinamide, N6-[[2-[[3-[[2-[(carboxymethyl)amino]-2-oxoethyl]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]ethoxy]ethoxy]acetyl]-N2-(1-naphthalenylacetyl)-L-lysyl-N6-[[2-[[3-[[2-[(carboxymethyl)amino]-2-oxoethyl]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]ethoxy]ethoxy]acetyl]-L-lysyl-N6-[[2-[[3-[[2-[(carboxymethyl)amino]-2-oxoethyl]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]ethoxy]ethoxy]acetyl]-L-lysyl-N6-[[2-[[3-[[2-[(carboxymethyl)amino]-2-oxoethyl]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]ethoxy]ethoxy]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

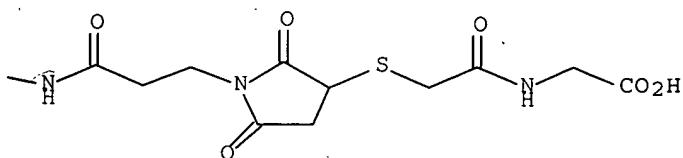
PAGE 1-A



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PAGE 1-C



L106 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:1026829 CAPLUS Full-text  
 DOCUMENT NUMBER: 143:312021  
 TITLE: Improved efficacy of targeted pharmaceutical  
 particulate agents with decoy systems  
 INVENTOR(S): Lanza, Gregory M.; Wickline, Samuel A.  
 PATENT ASSIGNEE(S): Barnes-Jewish Hospital, USA  
 SOURCE: PCT Int. Appl., 27 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005086639	A2	20050922	WO 2005-US4858	20050210
WO 2005086639	A3	20051124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005220706	A1	20050922	AU 2005-220706	20050210
CA 2555343	A1	20050922	CA 2005-2555343	20050210
EP 1720521	A2	20061115	EP 2005-749878	20050210
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007523090	T	20070816	JP 2006-553351	20050210
PRIORITY APPLN. INFO.:			US 2004-543761P	P 20040210
			WO 2005-US4858	W 20050210

AB A decoy inactive drug carrier composition is administered simultaneously with a targeted composition containing vehicles for delivering a desired agent to a biol. target. This simultaneous administration enhances the delivery of the targeted composition to the desired location in a subject. The co-administration of decoys extends the circulatory longevity of the indium-labeled particles which allows greater time for binding and signal enrichment at the target. To acquire the same level of signal at the target without decoys would require injecting far more, arguably unsafe levels, of indium-labeled particles to compensate for RES losses.

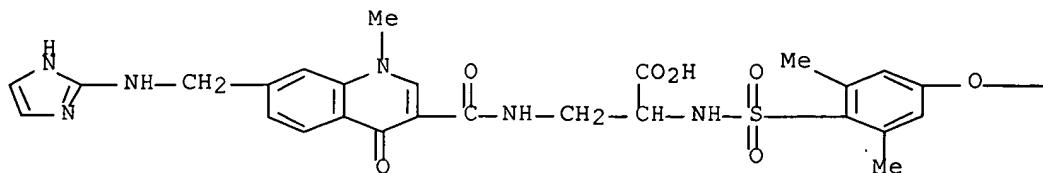
IT 569328-05-8P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (improved efficacy of targeted pharmaceutical particulate agents with decoy systems)

RN 569328-05-8 CAPLUS

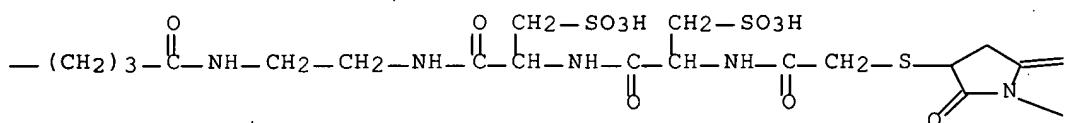
CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[[[(10R)-7-hydroxy-7-oxido-2,13-dioxo-10-[(1-oxooctadecyl)oxy]-6,8,12-trioxa-3-aza-7-phosphatriacont-1-yl]oxy]- $\omega$ -hydroxy-,  $\omega$ -ether with N-[[[1-[3-[(2-hydroxyethyl)amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]thio]acetyl]-3-sulfo-L-alanyl-N-[2-[[4-[4-[[[(1S)-1-carboxy-2-[[[1,4-dihydro-7-[(1H-imidazol-2-ylamino)methyl]-1-methyl-4-oxo-3-quinolinyl]carbonyl]amino]ethyl]amino]sulfonyl]-3,5-dimethylphenoxy]-1-oxobutyl]amino]ethyl]-3-sulfo-L-alaninamide, monosodium salt (9CI) (CA INDEX NAME)

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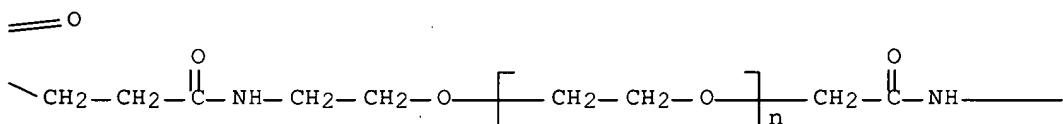


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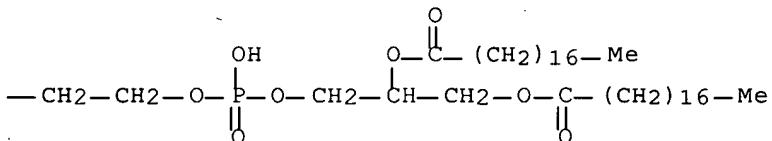
PAGE 1-B



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L106 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:35005 CAPLUS Full-text  
 DOCUMENT NUMBER: 142:133052  
 TITLE: Immunogenic conjugates comprising oligo- or poly-saccharide and carrier protein or peptide as vaccines against infection by *Shigella flexneri*  
 INVENTOR(S): Phalipon, Armelle; Nato, Farida; Mulard, Laurence; Sansonetti, Philippe  
 PATENT ASSIGNEE(S): Institut Pasteur, Fr.; INSERM Institut de la Sante et

de la Recherche Medicale; Centre National de la  
Recherche Scientifique; Baleux, Francoise; Belot,  
Frederic; Grandjean, Cyrille

SOURCE: PCT Int. Appl., 192 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent  
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003775	A2	20050113	WO 2004-IB2657	20040702
WO 2005003775	A3	20050506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2434685	A1	20050104	CA 2003-2434685	20030704
CA 2434668	A1	20050104	CA 2003-2434668	20030707
CA 2470262	A1	20050104	CA 2004-2470262	20040702
CA 2531023	A1	20050113	CA 2004-2531023	20040702
EP 1642132	A2	20060405	EP 2004-744281	20040702
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
IN 2005DN06026	A	20080711	IN 2005-DN6026	20051223
US 20080112951	A1	20080515	US 2006-563221	20060613
PRIORITY APPLN. INFO.:			CA 2003-2434685	A 20030704
			CA 2003-2434668	A 20030707
			WO 2004-IB2657	W 20040702

AB A conjugate mol. comprising an oligo- or polysaccharide covalently bound to a carrier and its use as potential vaccine against infection by S. Flexneri, especially type 2a. The oligosaccharides or polysaccharides are tetrasaccharides, pentasaccharides or their oligomers such as decasaccharides or penta-decasaccharides. The carrier protein or peptide is PADRE, tetanus toxoid, T cell epitope, or biotin. The glycoconjugates are especially useful for diagnosing and treating Shigellosis or Shigella flexneri infection in mammal and human.

IT 824939-76-6

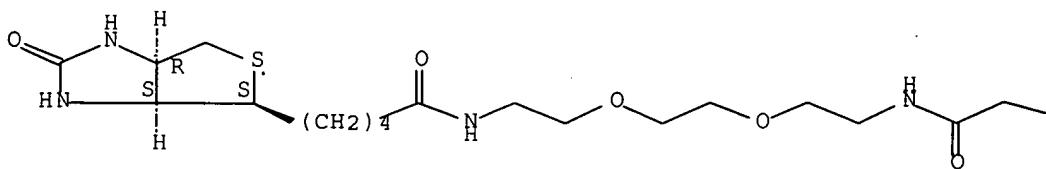
RL: RCT (Reactant); RACT (Reactant or reagent)  
(immunogenic conjugates comprising oligo- or poly-saccharide and carrier protein or peptide as vaccines against infection by Shigella flexneri)

RN 824939-76-6 CAPLUS

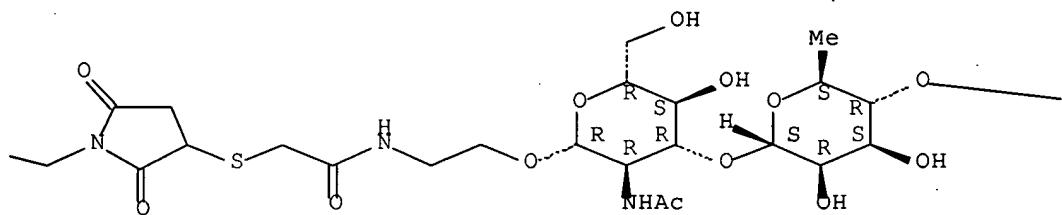
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[2-[2-[2-[[3-[3-[[2-[[O-  
α-D-glucopyranosyl-(1→4)-O-6-deoxy-α-L-mannopyranosyl-  
(1→3)-2-(acetylamino)-2-deoxy-β-D-  
glucopyranosyl]oxy]ethyl]amino]-2-oxoethyl]thio]-2,5-dioxo-1-pyrrolidinyl]-  
1-oxopropyl]amino]ethoxy]ethoxy]ethyl]hexahydro-2-oxo-, (3aS,4S,6aR)- (CA  
INDEX NAME)

Absolute stereochemistry.

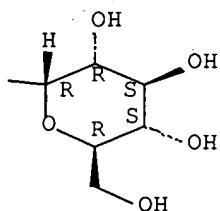
PAGE 1-A



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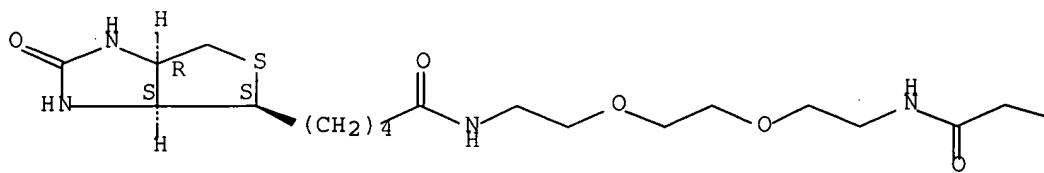


IT 824939-77-7P 824939-78-8P 824939-79-9P  
 824939-80-2P 824939-81-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (immunogenic conjugates comprising oligo- or poly-saccharide and carrier protein or peptide as vaccines against infection by *Shigella flexneri*)

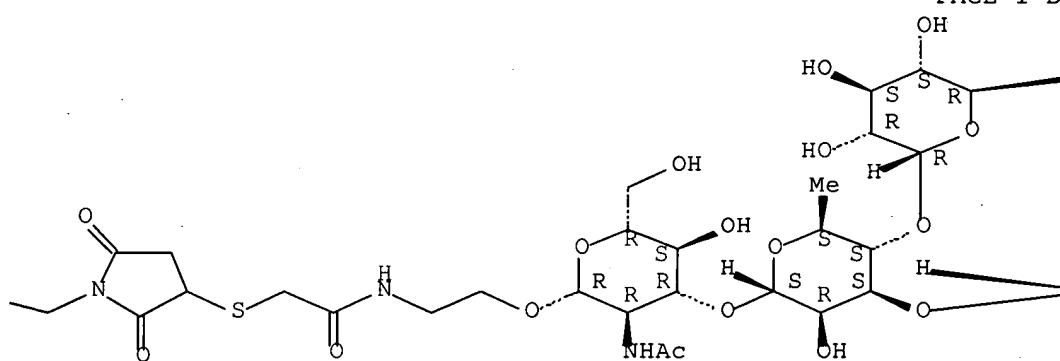
RN 824939-77-7 CAPLUS  
 CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[2-[2-[2-[3-[2-[2-[O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 3)-O- [ $\alpha$ -D-glucopyranosyl-(1 $\rightarrow$ 4)]-O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 3)-2-(acetylamino)-2-deoxy- $\beta$ -D-glucopyranosyl]oxy]ethyl]amino]-2-oxoethyl]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]ethoxy]ethoxy]ethyl]hexahydro-2-oxo-, (3aS,4S,6aR) - (CA INDEX NAME)

Absolute stereochemistry.

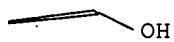
PAGE 1-A



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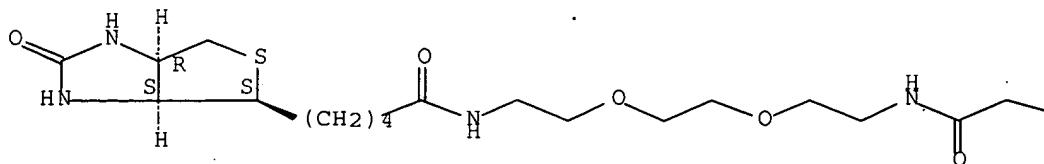


RN 824939-78-8 CAPLUS  
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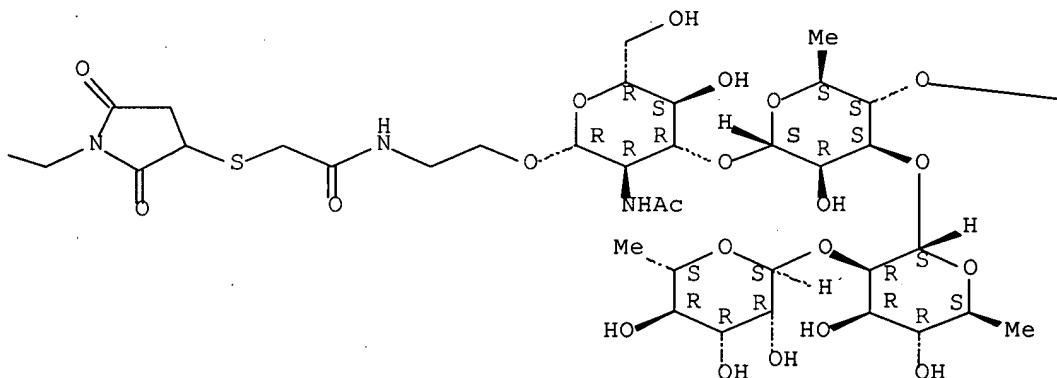
D-glucopyranosyl]oxy]ethyl]amino]-2-oxoethyl]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]ethoxy]ethoxy]ethyl]hexahydro-2-oxo-, (3aS,4S,6aR)- (CA INDEX NAME)

Absolute stereochemistry.

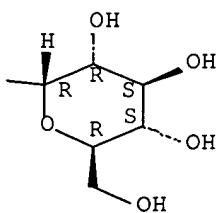
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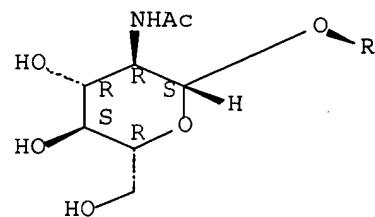
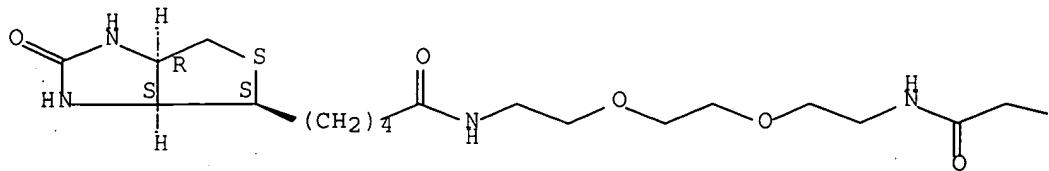
RN 824939-79-9 CAPLUS

CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[2-[2-[2-[3-[3-[2-[2-[O-2-(acetylamino)-2-deoxy-β-D-glucopyranosyl-(1→2)-O-6-deoxy-α-L-mannopyranosyl-(1→2)-O-6-deoxy-α-L-mannopyranosyl-(1→3)-O-[α-D-glucopyranosyl-(1→4)]-O-6-deoxy-α-L-mannopyranosyl-(1→3)-2-(acetylamino)-2-deoxy-β-D-

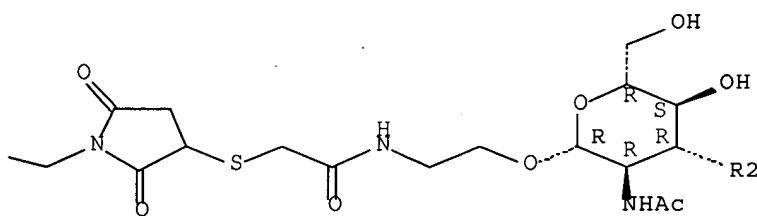
glucopyranosyl]oxy]ethyl]amino]-2-oxoethyl]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]ethoxy]ethoxy]ethyl]hexahydro-2-oxo-, (3aS,4S,6aR)- (CA INDEX NAME)

## Absolute stereochemistry.

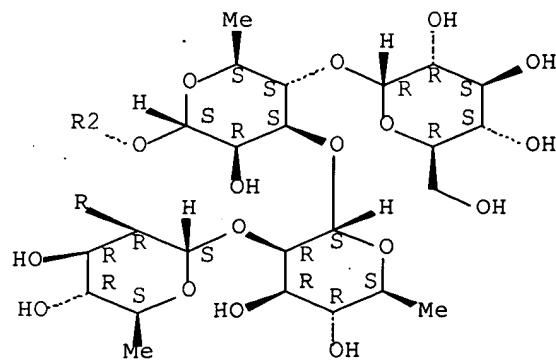
PAGE 1-A



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PAGE 2-A

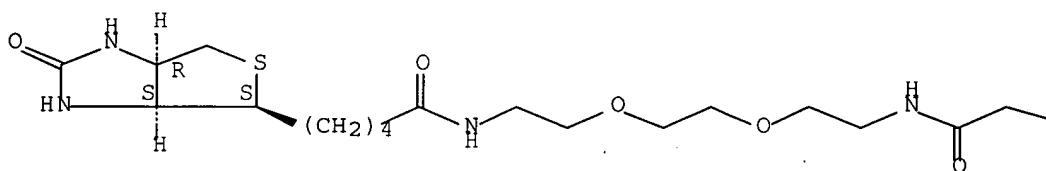


RN 824939-80-2 CAPLUS

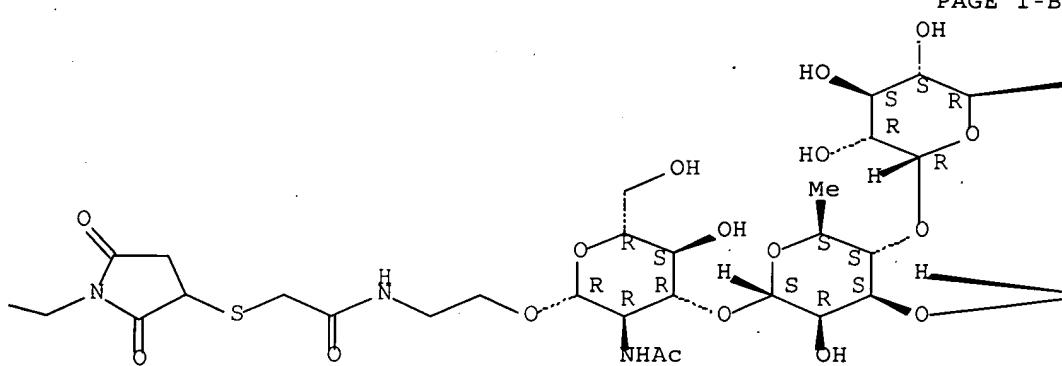
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[2-[2-[2-[3-[3-[2-[2-[2-[O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 2)-O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 3)-O-[ $\alpha$ -D-glucopyranosyl-(1 $\rightarrow$ 4)]-O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 3)-O-2-(acetylamino)-2-deoxy- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 2)-O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 3)-O-[ $\alpha$ -D-glucopyranosyl-(1 $\rightarrow$ 4)]-O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 3)-2-(acetylamino)-2-deoxy- $\beta$ -D-glucopyranosyl]oxyethyl]amino]-2-oxoethyl]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]ethoxy]ethoxyethyl]hexahydro-2-oxo-, (3aS,4S,6aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

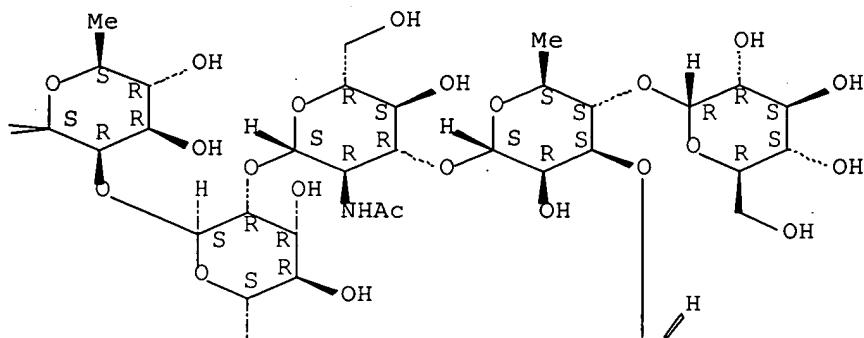
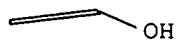
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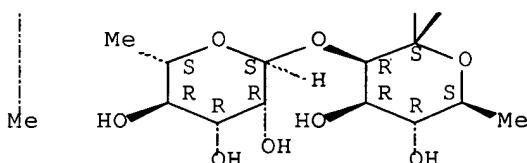
PAGE 1-B



PAGE 1-C



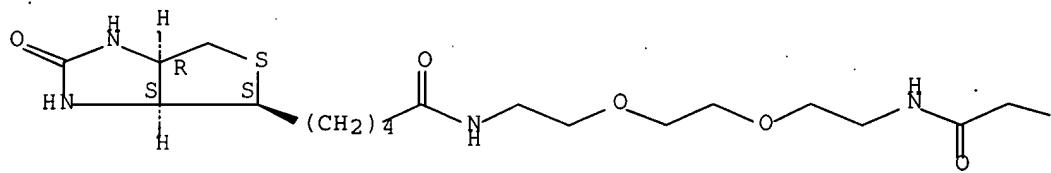
PAGE 2-C



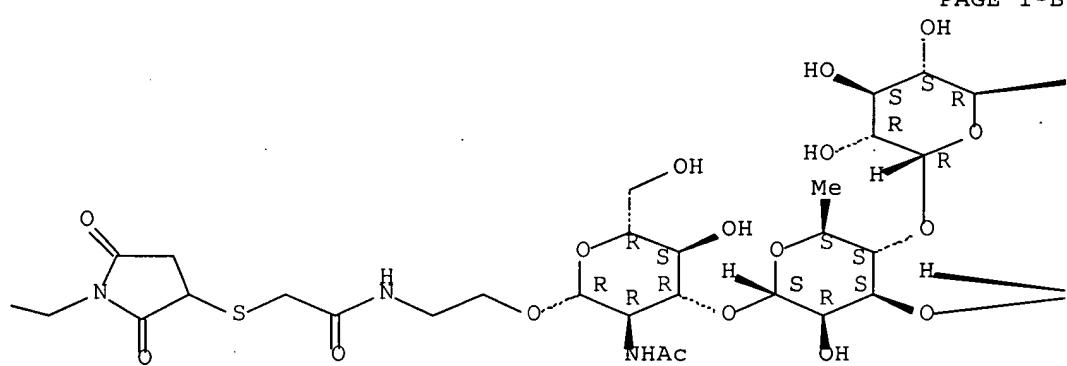
RN 824939-81-3 CAPLUS  
 CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[2-[2-[2-[3-[3-[2-[2-[[[O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 2)-O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 3)-O- $\alpha$ -D-glucopyranosyl-(1 $\rightarrow$ 4)]-O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 3)-O-2-(acetylamino)-2-deoxy- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 2)]2-O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 2)-O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 3)-O- $\alpha$ -D-glucopyranosyl-(1 $\rightarrow$ 4)]-O-6-deoxy- $\alpha$ -L-mannopyranosyl-(1 $\rightarrow$ 3)-2-(acetylamino)-2-deoxy- $\beta$ -D-glucopyranosyl]oxy]ethyl]amino]-2-oxoethyl]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]ethoxyethoxyethylhexahydro-2-oxo-, (3aS,4S,6aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

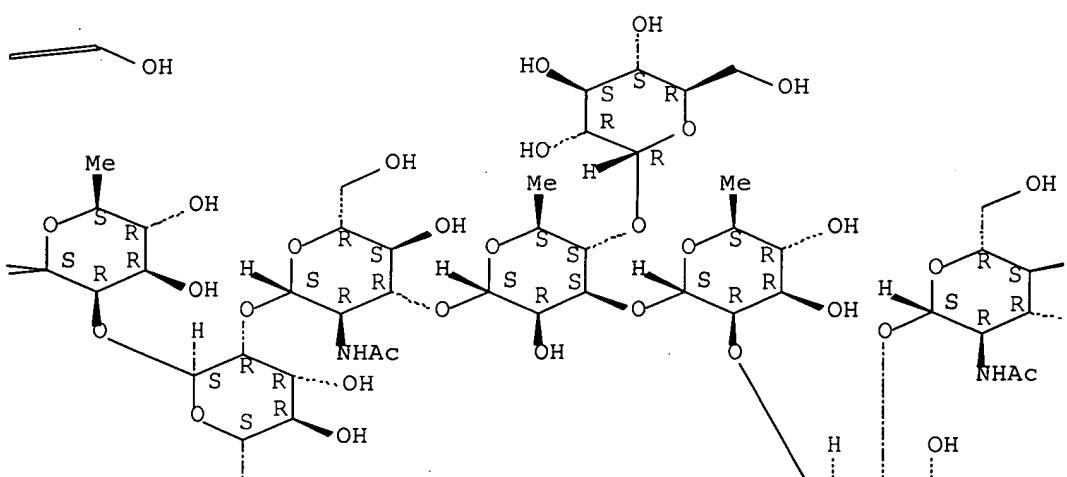
PAGE 1-A



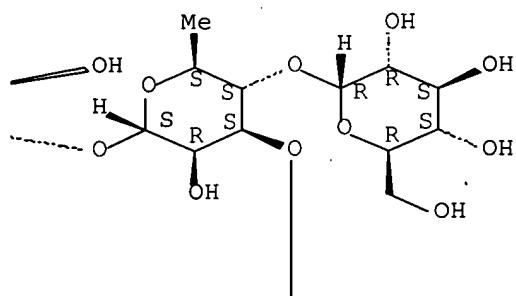
PAGE 1-B



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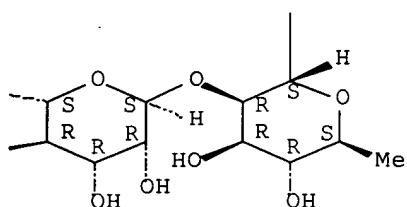
PAGE 1-D



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PAGE 2-D



L106 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2003:591145 CAPLUS Full-text  
 DOCUMENT NUMBER: 139:138724  
 TITLE: Integrin targeted imaging agents  
 INVENTOR(S): Lanza, Gregory; Wickline, Samuel A.; Harris, Tom  
 PATENT ASSIGNEE(S): Barnes Jewish Hospital, USA; Bristol-Myers Squibb Medical Imaging, Inc.  
 SOURCE: PCT Int. Appl., 64 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062198	A2	20030731	WO 2003-US2380	20030124
WO 2003062198	A3	20050804		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW		
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
CA 2474386	A1	20030731	CA 2003-2474386	20030124
BR 2003007206	A	20041221	BR 2003-7206	20030124
JP 2005525319	T	20050825	JP 2003-562080	20030124
EP 1572639	A1	20050914	EP 2003-707550	20030124
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TR 200401834	T2	20051021	TR 2004-1834	20030124
CN 1738815	A	20060222	CN 2003-806857	20030124
NZ 534500	A	20070727	NZ 2003-534500	20030124
MX 2004PA07188	A	20051018	MX 2004-PA7188	20040723
IN 2004KN01078	A	20061201	IN 2004-KN1078	20040728
ZA 2004006686	A	20050919	ZA 2004-6686	20040823
US 20080175792	A1	20080724	US 2008-971818	20080109
PRIORITY APPLN. INFO.:			US 2002-351390P	P 20020124
			US 2003-351463	A3 20030124
			WO 2003-US2380	W 20030124
			US 2005-305416	A1 20051216

OTHER SOURCE(S): MARPAT 139:138724

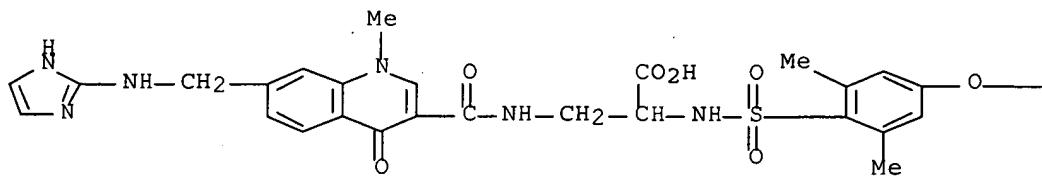
AB Emulsions preferably of nanoparticles formed from high boiling liquid perfluorochem. substances, said particles coated with a lipid/surfactant coating are made specific to regions of activated endothelial cells by coupling said nanoparticles to a ligand specific for  $\alpha v\beta 3$  integrin, other than an antibody. The nanoparticles may further include biol. active agents, radionuclides, or other imaging agents. Examples are provided of tumor, atherosclerosis and carotid balloon injury MRI using  $\alpha v\beta 3$  integrin-targeting nanoparticles comprising, in addition to the targeting agent, a gadolinium chelate.

IT 569328-05-8P  
 RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (integrin targeted imaging and therapeutic agents)

RN 569328-05-8 CAPLUS

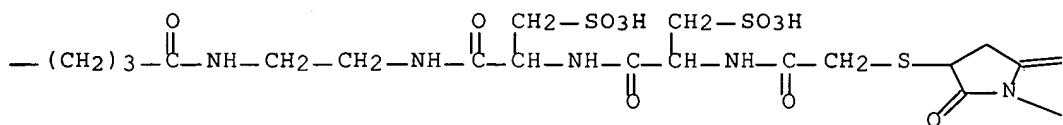
CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[[[(10R)-7-hydroxy-7-oxido-2,13-dioxo-10-[(1-oxooctadecyl)oxy]-6,8,12-trioxa-3-aza-7-phosphatriacont-1-yl]oxy]- $\omega$ -hydroxy-,  $\omega$ -ether with N-[[[1-[3-[(2-hydroxyethyl)amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]thio]acetyl]-3-sulfo-L-alanyl-N-[2-[[4-[4-[[[(1S)-1-carboxy-2-[[[1,4-dihydro-7-[(1H-imidazol-2-ylamino)methyl]-1-methyl-4-oxo-3-quinolinyl]carbonyl]amino]ethyl]amino]sulfonyl]-3,5-dimethylphenoxy]-1-oxobutyl]amino]ethyl]-3-sulfo-L-alaninamide, monosodium salt (9CI) (CA INDEX NAME)

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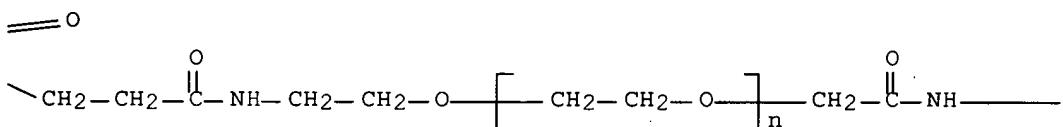


● Na

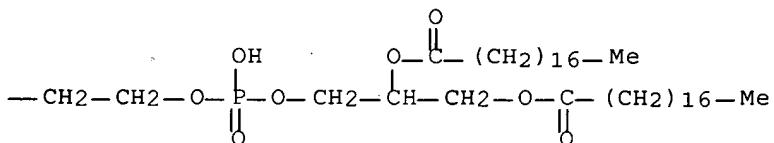
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L106 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2001:851403 CAPLUS Full-text  
 DOCUMENT NUMBER: 136:1626  
 TITLE: Labelling of vectors for DNA delivery with non-covalently bound polyamides carrying an affinity label for a target cell type  
 INVENTOR(S): Pessi, Antonello; Fattori, Daniela; Ingallinella, Paolo; Bianchi, Elisabetta; Kinzel, Olaf  
 PATENT ASSIGNEE(S): Istituto di Ricerche di Biologia Molecolare P.

SOURCE: Angeletti, S.p.A., Italy  
 PCT Int. Appl., 98 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

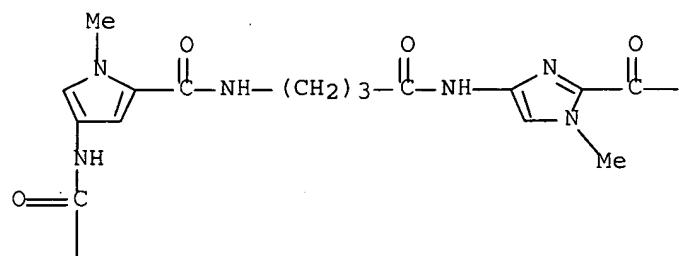
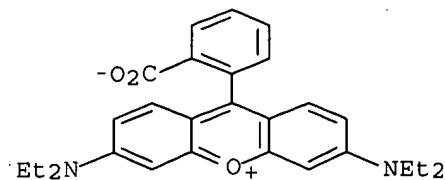
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001088160	A2	20011122	WO 2001-IB980	20010511
WO 2001088160	A3	20020725		
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2408885	A1	20011122	CA 2001-2408885	20010511
EP 1290198	A2	20030312	EP 2001-932034	20010511
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
US 20030207400	A1	20031106	US 2003-276734	20030512
PRIORITY APPLN. INFO.:			GB 2000-11938	A 20000517
			WO 2001-IB980	W 20010511

AB The present invention pertains to novel products suitable for use as gene delivery systems in which nucleic acid is linked to a ligand in order to facilitate delivery of the nucleic acid to a target cell or sub-cellular compartment via uptake of the ligand. More particularly, the present invention pertains to vectors comprising: (a) a double stranded DNA (dsDNA) having at least one target sequence; and, (b) a chimeric mol. comprising: (i) a sequence specific polyamide (SSP) moiety bound non-covalently to said target sequence; and, (ii) a ligand moiety linked covalently to said sequence specific polyamide. The polyamide may be a peptide, but not necessarily. The present invention also pertains to compns. comprising such chimeric mols. and vectors; methods for making such chimeric mols. and vectors; and methods of using such chimeric mols. and vectors, e.g., to deliver nucleic acid vectors to cells or sub-cellular compartments. Synthesis of polyamides labeled with dyes or polysaccharide ligand groups is described.

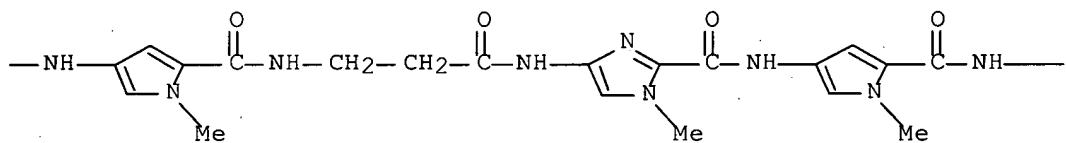
IT 375843-02-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and reactions of; labeling of vectors for DNA delivery with non-covalently bound polyamides carrying affinity label for target cell type)

RN 375843-02-0 CAPLUS  
 CN Xanthylium, 9-[2-carboxy-4(or 5)-[[[3-[[3-[[7-methyl-16-[1-methyl-4-[[1-methyl-4-[[3-[[1-methyl-4-[[1-methyl-4-[[4-[[1-methyl-4-[[1-methyl-4-[[1-methyl-1H-imidazol-2-yl]carbonyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]-1-oxopropyl]amino]-1H-imidazol-2-yl]carbonyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]-1-oxobutyl]amino]-1H-imidazol-2-yl]carbonyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]-1-oxopropyl]amino]-1H-imidazol-2-yl]carbonyl]amino]-1H-pyrrol-2-yl]-2,12,16-trioxo-3,7,11,15-tetraazahexadec-1-yl]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]propyl]amino]carbonyl]phenyl]-3,6-bis(diethylamino)-, inner salt (9CI) (CA INDEX NAME)

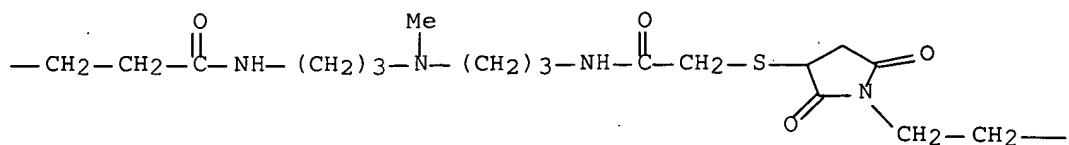
PAGE 1-A



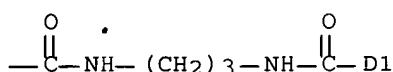
PAGE 1-B



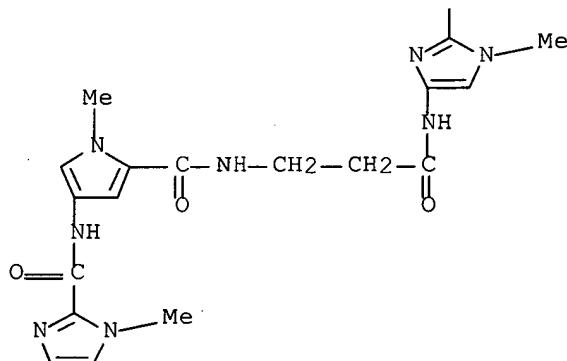
PAGE 1-C



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PAGE 2-A



L106 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2001:168004 CAPLUS Full-text  
 DOCUMENT NUMBER: 134:208057  
 TITLE: Oligosaccharides derived from ribose-ribitol-phosphate, and vaccines containing them  
 INVENTOR(S): Verez Bencomo, Vicente Guillermo; Roy, Rene  
 PATENT ASSIGNEE(S): Universidad de la Habana, Ministerio de Educacion Superior, Cuba; University of Ottawa  
 SOURCE: PCT Int. Appl., 50 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Spanish  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016146	A1	20010308	WO 2000-CU3	20000815
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CZ, DM, DZ, EE,				

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 MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, TR, TT,  
 UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 CA 2382602 A1 20010308 CA 2000-2382602 20000815  
 EP 1212334 A1 20020612 EP 2000-956040 20000815  
 EP 1212334 B1 20051102  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL  
 BR 2000013686 A 20020813 BR 2000-13686 20000815  
 JP 2003528032 T 20030924 JP 2001-519710 20000815  
 NZ 517464 A 20040326 NZ 2000-517464 20000815  
 AU 780816 B2 20050421 AU 2000-68173 20000815  
 AT 308551 T 20051115 AT 2000-956040 20000815  
 ES 2252045 T3 20060516 ES 2000-956040 20000815  
 MX 2002PA02066 A 20040730 MX 2002-PA2066 20020226  
 ZA 2002001667 A 20030527 ZA 2002-1667 20020227  
 IN 2002DN00258 A 20070921 IN 2002-DN258 20020228  
 KR 818163 B1 20080331 KR 2002-702706 20020228  
 US 6765091 B1 20040720 US 2002-70101 20020716  
 HK 1050693 A1 20050923 HK 2003-102864 20030423  
 IN 2005DN04592 A 20070817 IN 2005-DN4592 20051010  
 PRIORITY APPLN. INFO.: CU 1999-121 A 19990830  
 WO 2000-CU3 W 20000815  
 IN 2002-DN258 A3 20020228

AB The present invention relates to the field of medicine, in particular to the chemical synthesis of mixts. of oligosaccharides derived from ribose-ribitol-phosphate which are used as active principle in vaccines for the prevention of infections caused by Haemophilus influenzae type b (Hib), as well as to vaccines which comprise said mixture of oligosaccharides. The mixts. of oligosaccharides which have been obtained by chemical synthesis comprise repetitive units having the formula (phosphate-ribose-ribitol)<sub>n</sub> or (ribose-ribitol-phosphate)<sub>n</sub> of at least five compds. having structure A or B which represent the repetitive unit of the capsular polysaccharide of Haemophilus influenzae type b and differ only by n, n being higher than or equal to 4 and smaller than or equal to 25, and wherein R<sub>1</sub> or R<sub>2</sub> is a spacer for the conjugation to a carrier with the condition that R<sub>1</sub> = spacer if R<sub>2</sub> the = H, or R<sub>2</sub> = spacer if R<sub>1</sub> = H: (A), (B). The invention also relates to immunogens which contain said oligosaccharide mixts., to vaccines which contain said immunogens and to methods for preparing said oligosaccharides in the form of mixts. Furthermore, the invention relates to the use of the vaccines either sep. or combined to other vaccines for the prevention of infections caused by Haemophilus influenzae type b.

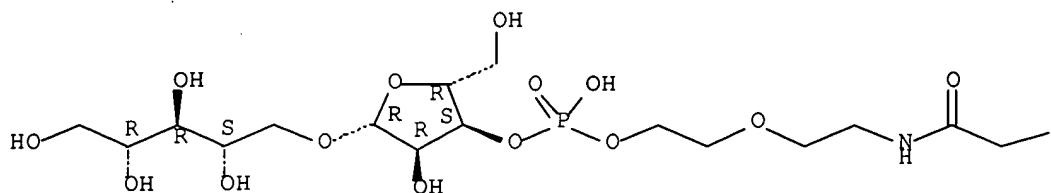
IT 329006-66-8DP, outer membrane protein conjugates  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (repeating unit, oligosaccharides derived from ribose-ribitol-phosphate, and vaccines containing them)

RN 329006-66-8 CAPLUS

CN D-Ribitol, 1-O-[3-O-[11-[3-[(3-amino-3-oxopropyl)thio]-2,5-dioxo-1-pyrrolidinyl]-1-hydroxy-1-oxido-9-oxo-2,5-dioxa-8-aza-1-phosphoundec-1-yl]-β-D-ribofuranosyl]-, monosodium salt (9CI) (CA INDEX NAME)

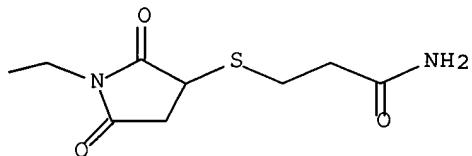
Absolute stereochemistry.

PAGE 1-A



Na

PAGE 1 - B



**REFERENCE COUNT:**

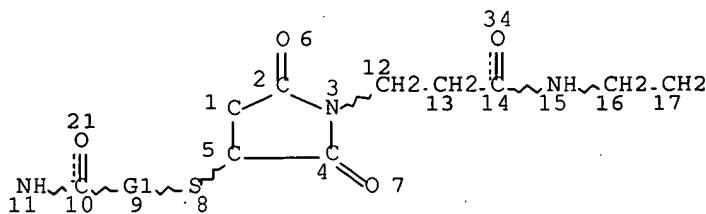
3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

FILE 'HOME' ENTERED AT 11:04:41 ON 30 JUL 2008

## SEARCH HISTORY

=> d stat que l105; d his nofile  
 L102 STR



$\text{CH}_2\sim\text{G}_1\sim\text{CH}_2 @23 \quad \text{CH}_2\sim\text{G}_2\sim\text{CH}_2 @25 \quad \text{CH}_2\sim\text{G}_3\sim\text{O}\sim\text{CH}_2\sim\text{CH}_2 @26 \quad @27 \quad @28 \quad @29 \quad @30 \quad \text{O}\sim\text{CH}_2\sim\text{CH}_2 @31 \quad @32 \quad @33$

VAR G1=CH2/23-10 25-8/26-10 30-8

REP G2=(0-8) CH2

REP G3=(0-9) 31-26 33-28

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

L105 25 SEA FILE=REGISTRY SSS FUL L102

100.0% PROCESSED 180 ITERATIONS

25 ANSWERS

SEARCH TIME: 00.00.01

(FILE 'HOME' ENTERED AT 09:00:23 ON 30 JUL 2008)

FILE 'CAPLUS' ENTERED AT 09:00:37 ON 30 JUL 2008

E US2004-634477/APPS

E US2003-634477/APPS

L1 1 SEA ABB=ON US2003-634477/AP  
 D SCAN  
 SEL RN

FILE 'REGISTRY' ENTERED AT 09:03:35 ON 30 JUL 2008

L2 1 SEA ABB=ON 11096-26-7  
 L3 1 SEA ABB=ON 209810-58-2  
 L4 7 SEA ABB=ON (11096-26-7/BI OR 113427-24-0/BI OR 122312-54-3/BI  
 OR 209810-58-2/BI OR 668496-68-2/BI OR 668496-69-3/BI OR  
 7439-89-6/BI)  
 L5 5 SEA ABB=ON L4 NOT (L2 OR L3)  
 D SCAN  
 D SCAN L3  
 D SCAN L2  
 L6 1 SEA ABB=ON 7439-89-6  
 E POLYETHYLENE GLYCOL/CN

L7           1 SEA ABB=ON POLYETHYLENE GLYCOL/CN

FILE 'CAPLUS' ENTERED AT 09:05:03 ON 30 JUL 2008

L8           448 SEA ABB=ON LEHMANN P?/AU  
 L9           9 SEA ABB=ON ROEDDINGER R?/AU  
 L10          2183 SEA ABB=ON WALTER MATSUI R?/AU OR WALTER R?/AU OR MATSUI  
               R?/AU

L11          12091 SEA ABB=ON L2  
 L12          441 SEA ABB=ON L2/D  
 L13          452 SEA ABB=ON L3  
 L14          472091 SEA ABB=ON L6  
 L15          108470 SEA ABB=ON L7  
 L16          35957 SEA ABB=ON PEG?/OBI  
 L17          38 SEA ABB=ON (L13 OR (L12 AND (L15 OR L16))) AND L14  
 L18          128446 SEA ABB=ON DIABET?/OBI  
 L19          4 SEA ABB=ON L17 AND L18.  
               D SCAN TI  
               D SCAN  
               D SCAN L1

L20          29210 SEA ABB=ON GLYCOSYLAT?/OBI  
 L21          25 SEA ABB=ON (L11 AND (L16 OR L20)) AND L18  
 L22          991257 SEA ABB=ON IRON/OBI  
 L23          29660 SEA ABB=ON ANEMI?/OBI  
 L24          6854 SEA ABB=ON RETICULOCYT?/OBI  
 L25          14 SEA ABB=ON (L11 AND (L16 OR L20 OR L15)) AND L18 AND (L14 OR  
               L22 OR L23 OR L24)  
               D SCAN TI  
 L26          1 SEA ABB=ON DEGREE/TI AND L25  
               D SCAN  
               D QUE L25  
 L27          12741 SEA ABB=ON ERYTHROPOIETIN/OBI  
 L28          2577 SEA ABB=ON EPO/OBI  
 L29          403 SEA ABB=ON (L27 OR L28 OR L14) (L) (L16 OR L20 OR L15)  
 L30          14 SEA ABB=ON L29 AND L18  
               D QUE  
 L31          8 SEA ABB=ON L29 AND L18 AND (L22 OR L23 OR L24 OR L14)  
 L32          12 SEA ABB=ON (L27 OR L28 OR L11) (L) (L16 OR L14 OR L20) AND L18  
               AND (L22 OR L23 OR L24 OR L14)  
               D SCAN TI HITIND  
               D QUE  
               D QUE L14  
               D QUE L13  
               D QUE L12  
 L33          4 SEA ABB=ON (L27 OR L28 OR L11) (L) (L15 OR L16 OR L20) AND L18  
               AND (L22 OR L23 OR L24 OR L14)  
               D SCAN TI  
               D SCAN TI L19  
 L34          8 SEA ABB=ON L13 AND L18 AND (L22 OR L23 OR L24 OR L14)  
 L35          6 SEA ABB=ON L34 NOT L33  
               D SCAN TI  
 L36          4 SEA ABB=ON L33 OR (L33 AND L13)  
 L37          3 SEA ABB=ON (L1 OR L8 OR L9 OR L10) AND ((L12 OR L13) OR (L11  
               AND (L15 OR L16 OR L20)))

FILE 'WPIX' ENTERED AT 09:33:04 ON 30 JUL 2008

L38          882 SEA ABB=ON WALTER MATSUI R?/AU OR WALTER R?/AU OR MATSUI  
               R?/AU  
 L39          7 SEA ABB=ON ROEDDINGER R?/AU  
 L40          190 SEA ABB=ON LEHMANN P?/AU  
 L41          3 SEA ABB=ON L38 AND L39 AND L40

D TRIAL 1-3

L42 2477 SEA ABB=ON ERYTHROPOIETIN/BI, ABEX  
L43 1121 SEA ABB=ON EPO/BI, ABEX  
L44 12 SEA ABB=ON DARBEPOIETIN/BI, ABEX  
L45 49879 SEA ABB=ON DIABET?/BI, ABEX  
L46 30843 SEA ABB=ON PEG?/BI, ABEX  
L47 51402 SEA ABB=ON POLYETHYLENEGLYCOL/BI, ABEX OR POLY/BI, ABEX (W) (ETHYL  
ENE GLYCOL/BI, ABEX OR ETHYLENE GLYCOL/BI, ABEX) OR POLYETHYLENE  
GLYCOL/BI, ABEX  
L48 4420 SEA ABB=ON GLYCOSYLAT?/BI, ABEX  
L49 78 SEA ABB=ON (L42 OR L43) AND L45 AND (L46 OR L47 OR L48)  
L50 0 SEA ABB=ON L44 AND L45 AND (L46 OR L47 OR L48)  
L51 7 SEA ABB=ON L44 AND (L45 OR L46 OR L47 OR L48)  
D SCAN  
L52 10 SEA ABB=ON (L42 OR L43) (8A) (L46 OR L47 OR L48) AND L45  
L53 264038 SEA ABB=ON IRON/BI, ABEX  
L54 6529 SEA ABB=ON ANEMI?/BI, ABEX  
L55 494 SEA ABB=ON RETICULOCYT?/BI, ABEX  
L56 26 SEA ABB=ON HEMOSIDER?/BI, ABEX  
L57 303 SEA ABB=ON HEMOCHROMATO?/BI, ABEX  
L58 29 SEA ABB=ON HAEMOSIDER?/BI, ABEX  
L59 81 SEA ABB=ON HAEMOCHROMATO?/BI, ABEX  
D QUE L52  
L60 30 SEA ABB=ON L49 AND (L53 OR L54 OR L55 OR L56 OR L57 OR L58 OR  
L59)  
L61 20 SEA ABB=ON (L42 OR L43) (S) (L46 OR L47 OR L48) AND L45 AND  
(L53 OR L54 OR L55 OR L56 OR L57 OR L58 OR L59)  
L62 4 SEA ABB=ON (L42 OR L43) (8A) (L46 OR L47 OR L48) AND L45 AND  
(L53 OR L54 OR L55 OR L56 OR L57 OR L58 OR L59)  
D SCAN  
L63 545 SEA ABB=ON L53 (3A) DISTRIBUT?/BI, ABEX  
L64 5 SEA ABB=ON (L42 OR L43 OR L44) AND L63  
D SCAN  
L65 913 SEA ABB=ON L53 (3A) (STOR?/BI, ABEX OR METABOLI?/BI, ABEX)  
L66 13 SEA ABB=ON (L42 OR L43 OR L44) AND L65  
L67 12 SEA ABB=ON L66 NOT (L41 OR L62 OR L64)  
D SCAN  
L68 30878 SEA ABB=ON OVERLOAD?/BI, ABEX  
L69 4 SEA ABB=ON (L42 OR L43 OR L44) AND L65 AND L68  
D SCAN  
L70 2 SEA ABB=ON (L42 OR L43 OR L44) AND L65 AND L68 NOT ANTIBOD?/BI  
, ABEX  
D SCAN

FILE 'MEDLINE' ENTERED AT 09:47:09 ON 30 JUL 2008

L71 1077 SEA ABB=ON WALTER MATSUI R?/AU OR WALTER R?/AU OR MATSUI  
R?/AU  
L72 0 SEA ABB=ON ROEDDINGER R?/AU  
L73 382 SEA ABB=ON LEHMANN P?/AU  
L74 13344 SEA ABB=ON IRON METABOLISM DISORDERS+NT/CT  
L75 16537 SEA ABB=ON ERYTHROPOIETIN+NT/CT  
L76 49008 SEA ABB=ON DIABETES MELLITUS, TYPE 2+NT/CT  
L77 2 SEA ABB=ON L74 AND L75 AND L76  
D TRIAL 1-2  
L78 9965 SEA ABB=ON IRON/CT(L)BL/CT  
L79 3 SEA ABB=ON L75 AND L76 AND L78  
D TRIAL 1-3  
L80 10150 SEA ABB=ON L75(L) (AD OR TU OR PD OR PK) /CT  
L81 1 SEA ABB=ON L80 AND L76 AND (L78 OR L74)

FILE 'STNGUIDE' ENTERED AT 09:51:17 ON 30 JUL 2008

FILE 'EMBASE' ENTERED AT 10:06:48 ON 30 JUL 2008

FILE 'MEDLINE' ENTERED AT 10:07:13 ON 30 JUL 2008

L82 0 SEA ABB=ON (L71 OR L72 OR L73) AND L75

FILE 'MEDLINE' ENTERED AT 10:07:33 ON 30 JUL 2008

L83 0 SEA ABB=ON (L71 OR L72 OR L73) AND (L75 OR L74 OR L78)

FILE 'EMBASE' ENTERED AT 10:08:02 ON 30 JUL 2008

L84 797 SEA ABB=ON WALTER MATSUI R?/AU OR WALTER R?/AU OR MATSUI  
R?/AU

L85 0 SEA ABB=ON ROEDDiger R?/AU

L86 417 SEA ABB=ON LEHMANN P?/AU  
E DIABETES MELLITUS, TYPE 2+ALL/CT

L87 53891 SEA ABB=ON NON INSULIN DEPENDENT DIABETES MELLITUS/CT  
E ERYTHROPOIETIN/CT  
E ERYTHROPOIETIN AN/CT  
E ERYTHROPOIETIN DER/CT  
E ERYTHROPOIETIN/CT  
E E3+ALL

L88 15072 SEA ABB=ON ERYTHROPOIETIN/CT OR ERYTHROPOIETIN DERIVATIVE/CT  
E IRON METABOLISM DISORDERS+ALL/CT

E E2+ALL

L89 7342 SEA ABB=ON IRON METABOLISM DISORDER+NT/CT  
E BLOOD IRON/CT  
E E3+ALL  
E E2+ALL

L90 3643 SEA ABB=ON IRON BLOOD LEVEL/CT

L91 1 SEA ABB=ON (L84 OR L85 OR L86) AND (L88 OR L89 OR L90)  
D TRIAL

L92 1 SEA ABB=ON L87 AND L88 AND (L89 OR L90)  
D TRIAL

FILE 'STNGUIDE' ENTERED AT 10:13:30 ON 30 JUL 2008

FILE 'CAPLUS' ENTERED AT 10:14:07 ON 30 JUL 2008  
D QUE L37

FILE 'WPIX' ENTERED AT 10:14:08 ON 30 JUL 2008  
D QUE L41

FILE 'MEDLINE' ENTERED AT 10:14:08 ON 30 JUL 2008  
D QUE L83

FILE 'EMBASE' ENTERED AT 10:14:08 ON 30 JUL 2008  
D QUE L91

FILE 'CAPLUS, WPIX, EMBASE' ENTERED AT 10:14:09 ON 30 JUL 2008  
L93 4 DUP REM L37 L41 L91 (3 DUPLICATES REMOVED)  
ANSWERS '1-3' FROM FILE CAPLUS  
ANSWER '4' FROM FILE EMBASE  
D IBIB AB HITIND 1-3  
D IALL 4

FILE 'MEDLINE' ENTERED AT 10:14:30 ON 30 JUL 2008  
D QUE L81

FILE 'EMBASE' ENTERED AT 10:15:03 ON 30 JUL 2008

D QUE L92

FILE 'CAPPLUS' ENTERED AT 10:15:03 ON 30 JUL 2008

D QUE L36

L94 3 SEA ABB=ON L36 NOT L37

FILE 'WPIX' ENTERED AT 10:15:03 ON 30 JUL 2008

D QUE L62

D QUE L64

D QUE L70

L95 7 SEA ABB=ON (L62 OR L64 OR L70) NOT L41

FILE 'STNGUIDE' ENTERED AT 10:15:09 ON 30 JUL 2008

FILE 'MEDLINE, CAPPLUS, WPIX, EMBASE' ENTERED AT 10:15:25 ON 30 JUL 2008

L96 12 DUP REM L81 L94 L95 L92 (0 DUPLICATES REMOVED)

ANSWER '1' FROM FILE MEDLINE

ANSWERS '2-4' FROM FILE CAPPLUS

ANSWERS '5-11' FROM FILE WPIX

ANSWER '12' FROM FILE EMBASE

D IALL 1

D IBIB AB HITIND 2-4

D IALL ABEX TECH 5-11

D IALL 12

FILE 'REGISTRY' ENTERED AT 10:45:30 ON 30 JUL 2008

L97 STRUCTURE uploaded

D QUE

L98 STR

L99 0 SEA SSS SAM L98

L100 STR L98

L101 0 SEA SSS SAM L100

L102 STR L100

L103 1 SEA SSS SAM L102

D SCAN

L104 180 SEA SSS FUL L102 EXTEND

L105 25 SEA SSS FUL L102

SAVE TEMP L105 ROB477FULL/A

FILE 'CAPPLUS' ENTERED AT 11:02:44 ON 30 JUL 2008

L106 11 SEA ABB=ON L105

D SCAN TI

D SCAN

FILE 'REGISTRY' ENTERED AT 11:04:24 ON 30 JUL 2008

D STAT QUE L105

FILE 'CAPPLUS' ENTERED AT 11:04:24 ON 30 JUL 2008

D QUE NOS L106

D IBIB ABS HITSTR L106 1-11

FILE 'HOME' ENTERED AT 11:04:41 ON 30 JUL 2008

D STAT QUE L105

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